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ON ACETIC ACID AS A SUBSTITUTE FOR ETHYL ALCOHOL IN EXTRACTING THE ACTIVE PRINCIPLES OF SOME OFFICINAL DRUGS.

By Edward R. Squibb, M.D.,
Of Brooklyn, N. Y.

(Third Paper, Belladonna Root.)

In continuing this subject for a third paper—see American Journal of Pharmacy for January, 1899, Vol. 71, No. 1, and Vol. 71, No. 7, for July, 1899, and *Ephemeris*, Vol. V, No. 3, for July, 1899, for the two preceding papers—the writer refers to without repeating the introductory matter of the first paper where the therapeutic and pharmaceutic bearings of the subject are discussed, and passes on to the farther work which is to be depended upon to support or oppose the proposed substitution, or ascertain the limits of its applicability.

The experimental trials and the actual use—chiefly in veterinary practice—of extracts and fluid extracts made with acetic acid have continued since the date of the last paper, until now the list embraces some sixty drugs and spices. This increasing experience tends to support two generalizations.

First, that a menstruum of 10 per cent. acetic acid is about the weakest that will surely extract, protect and preserve the active principles of many drugs, and that such a menstruum leaves not less than 6 nor more than 8 per cent. of free acid in the finished fluid extract, and is about equivalent as a menstruum to the officinal alcohol dilutum, or 41 per cent. alcohol.

Second, that from one-fourth to one-third of the fluid extracts

made with acetic acid give a small deposit within three months—a proportion not greater than from alcoholic menstrua, and that the deposits from the two menstrua are equally inert.

In selecting a third drug for competitive investigation in this paper, belladonna root was taken; first, on account of its importance; second, because its value depends on the proportion of a definite alkaloid of strong saturating power; and, third, because the writer has had much experience with it through many years.

In September, 1885, see *Ephemeris*, Vol. II, No. 11, pp. 848 and 853, the writer published papers on belladonna leaf and belladonna root, giving an assay process which, with slight modifications and with the addition of titration of the results, has now been in use for about fourteen years. This process is believed to be sufficiently accurate for all practical purposes, and is therefore adopted as the basis of this paper.[1]

An abstract of this process, as amended in recent practice, is as follows:

OLDER ASSAY PROCESS.

Fifty grammes of the unpeeled belladonna root in No. 60 powder was equally moistened with 30 c.c. of 91 per cent. alcohol to which 4 drops of concentrated sulphuric acid had been previously added.

The moistened powder was then moderately packed in a narrow cylindrical percolator and 100 c.c. of 91 per cent. alcohol, acidulated with 4 drops of sulphuric acid, was poured on top as fast as the percolator would hold it, a stratum of the menstruum being always kept on top. As soon as the powder was completely filled, and dropping began from below, the outlet was closed and a digestion of twenty-four hours was allowed.

The percolation was then started and maintained at a slow rate of dropping, stopping overnight for a new digestion, until 425 c.c. of percolate was received. The farther supply on top was 100 c.c. more of the alcohol acidulated with 4 drops of the acid, another 100

[1] The use of a good process of assay in the buying of an important drug through a series of years is well illustrated in the writer's experience with belladonna root. In 1885 the best root of the market gave 0·46 to 0·50 per cent. of alkaloids. In creating a demand by rejecting lower grade samples and calling for unpeeled root the quality obtainable has increased from about 0·50 per cent. to 0·68 per cent.

c.c. acidulated with 2 drops of acid, and then 200 c.c. of the alcohol not acidulated.

The percolate was boiled down in a flask on a water-bath to about 10 or 15 c.c. of liquid extract, and this was diluted and washed clean into a separator with 25 c.c. of water acidulated with 1 drop of acid. The flask was then finally rinsed into the separator with 20 c.c. of chloroform, 99 per cent.

The whole was well shaken for five minutes, allowed to separate and the chloroform layer drawn off into a second separator.

The acid liquid was again washed twice in the same way with 20 c.c. of chloroform.

The 60 c.c. of chloroform washings in the second separator was then washed by gentle shaking with 15 c.c. of water acidulated with 1 drop of acid, the chloroform stratum was drawn off and wasted, and the watery stratum was added to that in the first separator.

Then 20 c.c. of chloroform was added to the contents of the first separator, and 6 grammes of sodium carbonate added in small portions as long as effervescence was developed by shaking.

Then shook well for five minutes, allowed to separate and the chloroform stratum drawn off into a tared beaker.

This washing of the alkaline solution was repeated twice when the tared beaker contained about 60 c.c. of chloroform solution of crude alkaloids.

The chloroform was evaporated off without boiling and left an amber-colored varnish-like extract that weighed 0·38 gramme = 0·76 per cent. crude alkaloids.

Upon this extract in the beaker 12 c.c. of decinormal sulphuric acid was delivered from a burette and the beaker was heated in a hot water-bath with rotary agitation until the soluble part of the extract was dissolved.

Then decinormal solution of potassium hydrate was dropped into the acid solution. The indicator used was narrow (4 millimetres) strips of blue and neutral litmus paper, touching the tip end to the liquid and cutting off the wet portion at each testing. The dropping in was continued until the liquid produced no change of color on either strip. Then after each additional drop or half drop the testing was made with the neutral strip. This was first touched to water, which wetted about 1 centimetre of the end, and then was

touched to the solution and held in contact for about ten seconds. Then on close inspection a bluish tinge was perceptible, indicating the finished titration.

12 c.c. of decinormal acid had been taken and 0·30 c.c. of decinormal alkali had been required to saturate the uncombined acid, leaving 11·70 c.c. saturated by the alkaloid of belladonna.

The molecular weight of atropine being 288·38, the calculation for the result was:

·28838 × 11·70 = ·3374046 × 2 = ·67481 = ... 0·675 per cent.
Duplicate assay . . . . . 0·685 "

1·360 ÷ 2 =
·680 average

For the many assays needed in the design of this paper a shorter assay process was needed, and one that could be applied to the differing fractions of percolate without too much sacrifice in accuracy of results. Such a process the new acetic acid menstruum seems to have supplied by taking the basis or design of the older process and cutting out some steps that could be shown to be dispensable.

THE NEWER ASSAY PROCESS.

Ten grammes of the unpeeled belladonna root, in No. 60 powder, was equally moistened with 5 c.c. of 10 per cent. acetic acid, the moistened powder was lightly packed in an extractor—A. J. P., 1899, p. 312; *Ephemeris*, p. 2313—(or some equivalent percolator), was filled to saturation with 10 per cent. acetic acid, was allowed to digest for twenty-four hours, and was then percolated to exhaustion, yielding about 200 c.c. of percolate.

This percolate was evaporated on a hot water-bath to an extract that was hard when cold, and weighed 3·96 grammes.

This extract was dissolved in 20 c.c. of a mixture of equal volumes of 91 per cent. alcohol and 10 per cent. water of ammonia, the solution transferred to a separator, 20 c.c. of chloroform added, the whole well shaken for five minutes, allowed to separate and the chloroform stratum drawn off into a beaker.

During the time required for separating, the wetted end of a strip of neutral or acid litmus paper was held in the vapor space of the separator in order to be sure of the full alkalinity of the contents.

Then 4 c.c. of 91 per cent. alcohol was added to the contents of the separator and shaken in. Then 20 c.c. of fresh chloroform, five minutes' vigorous shaking, with separation and drawing off the chloroform stratum into the beaker as before.

This addition of alcohol and chloroform, shaking, separating and drawing off was repeated for a third and final washing.

The chloroform solution was evaporated from the beaker without boiling, leaving a varnish-like extract that weighed 0·15 gramme.

This was dissolved in 6 c.c. of decinormal acid by water-bath heat and agitation, and was titrated back with decinormal alkali to the neutral point, using litmus paper indicator in the way described in the old process.

6·00 c.c. acid used less 3·65 c.c. free acid = 2·35 c.c. saturated with alkaloid,
·28838 × 2·35 = ·67769 = ... 0·680 per cent.
Duplicate assay . . . . . 0·680 " "

These percentages are true only to the second decimal place, and are, therefore, so stated. But they are usually trustworthy to 0·005 per cent. It is claimed, however, that a simple and easy process that will give a result true within this first range of error is more practically useful than a more elaborate process with half that range of error.

This is equivalent to stating the writer's conviction, long held, that for pharmacopœial purposes a process that five pharmacists out of ten can apply within a variable error of 1 per cent. of result is of more use than a more elaborate process that not more than one in ten can apply to within half that range of error of result.

The new process has been applied to the percolates as well as to the powder with the same degree of success, 10 c.c. of the stronger percolates being evaporated for each assay, and multiples of this volume for the weaker percolates.

Throughout the many applications of the new process it was found that unless the proportion of solid extract was required it was better not to carry the evaporation lower than to a thick liquid of 5 or 6 grammes, because it is much easier to wash it clean into the separator with the prescribed volume of the ammonia-alcohol mixture.

The one great difficulty in applying the "shaking out" process in alkaloidal assaying is the formation of emulsions. This difficulty is entirely avoided in this process by the use of alcohol: First to

dilute the ammonia, and afterward to replace the alcohol shaken out by the chloroform in each washing of the alkaline liquid. When this was done as prescribed in the process the separation was always prompt and complete, and the chloroform solutions were all fairly clear.

In dissolving the alkaloids out from the crude alkaloids by the decinormal acid, for titration, care, patience, agitation and a hot water-bath are needed, and the heat must be sufficient to fuse the resinous matter that is liable to hold the alkaloid from the acid.

The principal limitation to the accuracy of the new process is in the use of litmus paper as an indicator. By the use of the tip end of very narrow strips very little of the solution is lifted out and cut off at each testing, but there is a point at which the solution does not change the color of either the blue or the neutral paper where sometimes one and sometimes two drops are required to produce a faint bluish tinge near the middle of the wetted end of the neutral strip, and this difference of one drop sometimes affects the result in the second decimal place of percentage. If the drops be divided, or if centinormal alkali be used when the neutral point is near, a closer result may be reached, but this latter introduces a complication, and only reduces the error by about one-half, or from about 1 in 60 to 1 in 120.

COMPARATIVE PERCOLATIONS.

Five hundred grammes of the same No. 60 powder of the unpeeled belladonna root was taken for each of two parallel percolations, the two being carried through under the same conditions of time and management as nearly as practicable.

For one percolation the U.S.P. menstruum, consisting of 800 volumes of 91 per cent. alcohol and 200 volumes of water, was used, and for the other 10 per cent. acetic acid.

Each portion of powder was moistened with 200 c.c. of its respective menstruum, both were digested in covered vessels for twenty-four hours—packed in syphon percolators—fully saturated with menstruum, and digested for twenty hours. Then the syphons were started at a slow rate of dropping, and, stopping overnight, were kept nearly parallel to the end.

The percolates were received in 100 c.c. fractions in 100 c.c. narrow-necked, marked flasks, and were weighed to 1 centigramme.

The 100 c.c. of the alcoholic U.S.P. menstruum weighed 86·91 grammes, and the 100 c.c. of the acid menstruum, 101·21 grammes.

These weights, subtracted from the differing weights of the fractions, give the difference between the weight of the menstruum and the weight of the fractions, and thus give a useful indication of the rate and degree of exhaustion. Each successive five fractions were

RATE AND DEGREE OF EXHAUSTION BY DIFFERENCES AND BY ASSAY.

Fractions of Percolate.	Differences.		Extract.		Chloroform Ext.		Alkaloids.	
	U.S.P. Menstruum.	Acetic Acid Menstruum.	U.S.P. Menstruum.	Acetic Acid Menstruum.	U.S.P. Menstruum.	Acetic Acid Menstruum.	U.S.P. Menstruum.	Acetic Acid Menstruum.
C.c.	Gms.	Gms.	P. C.	P. C.	P. C.	P. C.	P. C.	P. C.
1st. 100 . . .	3·82	13·57						
2d. 100 . . .	3·63	12·92						
3d. 100 . . .	3·70	10·79						
4th. 100 . . .	4·05	8·12						
5th. 100 . . .	4·59	5·36						
1st. 500 . . .	21·48	51·85	12·7	30·1	2·30	1·30	0·634	0·605
6th. 100 . . .	4·57	3·62						
7th. 100 . . .	3·59	1·46						
8th. 100 . .	2·77	·72						
9th. 100 . . .	2·39	·51						
10th. 100 . . .	1·99	·42						
2d. 500 . . .	17·45	7·27	6·5	4·2	0·30	0·45	0·036	0·072
11th. 100 . . .	1·46	·33						
12th. 100 . . .	·99	·30						
13th. 100 . . .	·81	·18						
14th. 100 . . .	·55	·19						
15th. 100 . . .	·43	·09						
3d. 500 . . .	5·33	1·13	2·0	0·7	0·10	0·06	0·007	0·006
16th. 100 . . .	·33	·06						
17th. 100 . . .	·14	·12						
18th. 100 . . .	·20	·09						
19th. 100 . . .	·00	·00						
20th. 100 . . .	·00	·00						
4th. 500 . . .	3·14	·26	1·1	0·5	0·10	0·06	0·006	0·005
							0·683	0·688

put together and made up to 500 c.c. from the next following percolate, the differences taken, the percentage of extract and chloroform extract taken, and the percolate assayed for the percentage of alkaloid by the new process, the drops being divided roughly in the titration so as to bring the result into the third decimal place of percentage.

All these results are summed up in the above table.

This powdered belladonna root gave, on careful assay by the older process, between 0·675 and 0·685 per cent. of alkaloid calculated as atropine, and it is accepted as being very near to a mean of 0·680 per cent. Then, as the results are practically the same by the newer process, the indication is confirmatory of both processes and of their common result—0·680 per cent.

In reviewing the table a very remarkable difference is shown in both the rate and degree of exhaustion. The acetic acid menstruum extracts more than three times as much in the earlier fractions, and exhausts the powder more rapidly and more completely throughout.

The two extracts differ in the same direction, both in rate and degree, so that it is surprising to find the alkaloids differing in an opposite direction.

The powder contains 0·680 per cent. of alkaloids.

The first 500 c.c. from the U.S.P. menstruum contains 93·23 per cent. of this.

The first 500 c.c. from the acid menstruum contains 88·97 per cent. of this.

The second 500 c.c. from the U.S.P. menstruum contains 5·29 per cent. of this.

The second 500 c.c. from the acid menstruum contains 10·58 per cent. of this.

The third 500 c.c. from the U.S.P. menstruum contains 1·03 per cent. of this.

The third 500 c.c. from the acid menstruum contains 0·88 per cent. of this.

The fourth 500 c.c. from the U.S.P. menstruum contains 0·88 per cent. of this.

The fourth 500 c.c. from the acid menstruum contains 0·74 per cent. of this.

Sum of the percentages U.S.P., 100·43; acid, 101·17 per cent.

Sum of the alkaloids U.S.P., 0·683; acid, 0·688 per cent.

Thus it will be seen that the U.S.P. menstruum gives the largest yield of alkaloid in the early part of the percolate and much the smallest yield of inert and useless extractive matter, and is so far the better menstruum, but, for washing out the last portion of alkaloid, the acid menstruum has a slight advantage.

The management is equally easy in both, and, when both are finished to fluid extract by the U.S.P. directions, the preparations appear to be of equal value. The acid preparation is of much lighter color, has no deposit in three months' standing, and does not precipitate on being added to water.

The alcoholic preparation is of a very dark color, has a small precipitate within three months that contains traces of alkaloid, and precipitates on being added to water.

The acid menstruum costs less than 2 cents a pint (473 c.c.).

The alcoholic menstruum costs more than 24 cents a pint.

THE HISTORY OF THE CONSTITUTION OF THE ALKALOIDS.

By A. R. L. Dohme, Ph.D.

An alkaloid is defined differently by different authorities on the subject, one set of chemists considering it to be a derivate of the base pyridine, while another set of chemists consider it to be a substance containing nitrogen and possessing basic properties. The former class, headed by Pictet, do hence not consider caffeine, theobromine, ethylamine, etc., as alkaloids, while the latter, headed by Guareschi, include these substances in the class of alkaloids. As stated in a paper published some years ago, I am inclined to take the broader view of the case and consider an alkaloid to be any nitrogenous substance possessing basic properties and forming stable salts. Although the great majority of the alkaloids, as we shall see, are derivatives of pyridine, it seems to me to be unscientific to assume that all alkaloids are such, or that there is any organic connection between alkaloidal property and pyridine, for the day may soon come when an alkaloid is discovered that is not a derivative of pyridine, and is yet a pronounced alkaloid in possessing alkaloidal properties and pronounced therapeutic activity. And I must confess to know of no reason why, by an arbitrary standard, such a

well-known therapeutic agent as caffeine should be excluded from the family of alkaloids. As is well known, the word alkaloid is derived from the Arabic word alkali and the Greek word Eidos, and means "like an alkali." The word alkali is derived from the Arabic words Al and Kali, meaning "the potash." Alkaloids are like an alkali because they resemble the typical alkali ammonia in possessing alkaline properties, forming stable salts and at times being volatile, as in case of nicotine or coniine. They are the organic bases. There are two classes of alkaloids, vegetable and animal, and at first, in the early part of this century, chemists only considered the vegetable alkaloids as bases, assuming that the animal body only excretes substances of neutral or acid character and never basic character. Thus Liebig classed such products as xanthine, creatine, etc., as members of the family of the starches. Alkaloids have always been closely associated with the term active principle, and whenever an alkaloid was isolated from a drug, it was promptly heralded as its active principle. This is, of course, not the case necessarily, for in some drugs that contain alkaloids the active principle, as far as the use of the drug is at present put to in medicine, is not an alkaloid. Because they were considered the active principles of drugs, their discovery was a great factor in the development both of chemistry and of medicine, for physicians saw in them the first means at their command of administering exact doses, and chemists saw in them the dawn of an era which would bring chemistry closely in touch with medicine, and thus ennoble the science of chemistry and at the same time greatly increase its usefulness and importance. The words uttered by the great physician, Claude Bernard, are hence strictly in accord with the trend of medical and pharmaceutical thought ever since, "La premiere condition de tout progres pour la medicine, c'est l'emploi de substances bien définies qu'on puisse doser exactement, et dont it soit possible de mésurer les effets." From this we see that Claude Bernard was the father of chemical assaying, for he says the first condition of all progress in medicine is the use of substances that are well defined, and whose effects can be measured and which can be administered in exact doses. It is a curious fact that as far as is known nearly all vegetable alkaloids are derivatives of a substance which is a closed chain, while nearly all animal alkaloids are derivatives of substances that are open chains. As you all know, the first alkaloid isolated from

any plant was morphine, and the honor of the discovery belongs to the German apothecary, Friedrich Wilhelm Sertürner, of the little town of Einbeck, near Hannover, who, in 1805, isolated the alkaloid morphine and recognized its basic character. Baume, in 1802, had isolated a substance from opium, which he called "sel essentiale opii," and which he found to be the active principle, and Derosne, in 1805, and Seguin, in 1804, had also separated such a substance in crystalline form and of decided narcotic nature, but neither of them recognized the alkaline nature of the same. Sertürner's views as to the alkalinity of morphine met with no favor at the time, and it was not until he made a second and more complete study and published a second paper on the subject in 1817, that the scientific world accepted the same with any degree of credence. Then all of a sudden it dawned on this scientific world that a new era had dawned for chemistry, and that an epoch-making discovery had been announced by the modest young pharmacist of Einbeck. So great an authority as Gay Lussac was stirred by its importance, and he says in the *Annales de Chimie et de Physique*, "Nous sommes surpris que le premier memoire de M. Sertürner nait pas fixé plus tot l'attention des chimistes, non en France, ou il ne parait pas qu'il ait été connu, mais sur le reste du continent. La decouverte d'une base alcaline formée de charbon, d'hydrogen, d'oxygene et d'azote, dans laquelle les propriétés neutralisantes sout tres prononcées, nous parait de la plus grande importance." Sertürner did the first part of his work at Paderborn, in Westphalia, and the latter part of it in Einbeck. He recognized, besides the basic nature of morphine, its powerful narcotic properties, and attributed the narcotic properties of opium to it. He also showed that ammonia and magnesia can displace it from its salts with acids, while it, when in this free state, can displace iron, lead, copper and mercury from their salts. The alkaloid era had set in, and from this year, 1817, until 1835, chemists labored incessantly on the new class of alkaloids, as the following list of discoveries of new alkaloids will demonstrate:

1817.	Morphine	By Sertürner.
	Emetine	" Pelletier and Magendie.
	Narcotine	" Robiquet.
1818.	Veratrine	" Meissner, Pelletier and Caventou.
	Strychnine	" Pelletier and Caventou.
1819.	Brucine	" " "
	Piperine	" Oersted.
	Delphinine	" Brandes.

1820.	Cinchonine	By Pelletier and Caventou.
	Quinine	" " "
	Solanine	" Desfosses.
1824.	Chelidonine	" Godefroy.
1826.	Corydaline	" Wackenroden.
	Berberine	" Chevallier and Pelletan.
1827.	Conicine	" Giesecke.
1828.	Nicotine	" Posselt and Reimann.
1829.	Aricine	" Pelletier and Corriol.
	Sanguinarine	" Dana.
1832.	Codeine	" Robiquet.
	Narceine	" Pelletier.
1833.	Quinidine	" Henry and Delondre.
	Atropine	" Geiger and Hesse.
	Hyoscyamine	" " "
	Aconitine	" " "
	Colchicine	" " "
1835.	Thebaine	" Pelletier and Thiboumery.

Every drug that possessed therapeutic virtue was examined for alkaloids, and as soon as these were isolated, they were examined by physiologists, who, in great number, were as much interested as the chemists. Magendie notably figured in these physiological experiments, as his celebrated "Formulaire," published in 1821, bears witness. Of these many publications, perhaps the most classical and complete is that of Pelletier and Caventou, on "Cinchonine and Quinine." The formula, *i. e.*, the composition of these alkaloids, was usually not determined by the investigator, but by the great analysts of the day—Liebig, Regnault, Laurent and Gerhardt. Knowing what the empirical formulas of these substances were, the next problem that naturally engaged the attention of the chemists was their constitution—how were these many atoms of these large and complex molecules combined and grouped. Two theories were at the time in vogue, and both were distinct and radically different. They were the conjugated theory of Berzelius and the amidogen theory of Liebig.

The former explained the constitution of the alkaloids by assuming that in them the ammonia was contained as such, and to it was conjugated the various radicals that caused the difference in properties, composition, etc., thus:

NH_3,	Ammonia.
$NH_3.CH_2$,	Methylamine, or methyliak.
$NH_3.C_2H_4$,	Ethylamine, or ethyliak.
$NH_3.C_5H_{11}$,	Nicotine.
$NH_3.C_6H_4$,	Aniline, etc., etc.

The latter, or Liebig's amidogen theory, assumed that all alkaloids contained the radical amidogen NH_2 and that they were really ammonia in which one hydrogen atom was replaced by an electropositive radical which was different for each alkaloid. This was in 1842. Both of these were merely the views or the theories of these two chemists. The first step in the illuminating of the ways was made by A. W. von Hofmann, a pupil of Liebig, and, strange to say, an adherent of the Berzelius alkaloid theory. It was in 1843 that Hofmann began his famous work on the substance aniline, which served the chemical world a twofold purpose—first, in establishing the aniline industry; and, secondly, in disproving the Berzelius alkaloid theory and establishing the Liebig theory of the constitution of these compounds. Unverdorben had in 1826 obtained a substance he called "Krystallin" by the dry distillation of indigo, and later, in 1840, Fritzsche, by distilling indigo with caustic potash, had obtained a substance, an oil, which he named aniline. Zinin, about the same time, obtained a substance he named "Benzidam," by the action of ammonium sulphide on nitrobenzene. You will note that I use the terminology *ene* for aromatic hydrocarbons, and not *ole*, as I frequently observe is done, and as is given in the U.S.P. Old and new teachers of chemistry give, as far as I know, the names benzene, toluene, xylene, etc., to these substances, and not benzole, toluole, xylole, etc., as the termination ole or ol is to be, and always has been, as far as I know, reserved for substances of an alcoholic nature, such as carbinol, phenol, resorcinol, etc., *i. e.*, such substances as contain hydroxyl. Hofmann, in 1843, fractionally distilled the heavy oil from coal tar, and obtained a colorless oil, which he called cyanol, and which he showed was identical with the krystallin, aniline and benzidam just mentioned. He tried the action of cyanogen upon aniline, and obtained cyananiline, cyano-diphenyl-diamine, or, as he called it, melaniline and dicyan-melaniline, all bases and addition products. He still thought that his work so far demonstrated the correctness of Berzelius' view of conjugated compounds, and he writes these compounds $NH_3.C_6H_4$, equivalent to aniline; $NH_3.C_6H_4.CN$ equivalent to cyananiline, etc. He now tried to split up aniline into ammonia and phenyl, its two conjugated radicals, but, of course, failed. He next applies a rigorous test to the Berzelius theory by studying the action of phosphorus pentoxide, a powerful dehydrating agent, upon oxanilide, arguing

that if this substance abstracts water from ammonium oxalate and yields cyanogen as a final product, why should it not yield anilocyanogen, as he calls it, from aniline oxalate.

$$\underset{\text{Ammon. Oxalate.}}{\begin{matrix}COONH_4\\ |\\ COONH_4\end{matrix}} - 2H_2O = \underset{\text{Urea.}}{\begin{matrix}CONH_2\\ |\\ CONH_2\end{matrix}} - 2H_2O = \underset{\text{Cyanogen.}}{\begin{matrix}CN\\ |\\ CN\end{matrix}} \quad \text{and}$$

$$\underset{\text{Aniline Oxalate.}}{\begin{matrix}COOH.C_6H_7N\\ |\\ COOH.C_6H_7N\end{matrix}} - 2H_2O = \underset{\text{Oxanilide.}}{\begin{matrix}CO.NHC_6H_5\\ |\\ CO.NHC_6H_5\end{matrix}} - 2H_2O = \underset{\text{Anilocyanogen.}}{\begin{matrix}CNC_6H_4\\ |\\ CNC_6H_4\end{matrix}}$$

He obtained all these products except the last—anilocyanogen, but never succeeded in getting it. Why this peculiar action of aniline? asks Hofmann. Berzelius' theory stays or falls with it; and, as it could not be coaxed into existence, Hofmann looks to Liebig's theory to explain the trouble, and at once sees that the last stage is impossible, since the last molecule of water could not be removed without splitting up the radical phenyl, and, as we all know, phenyl is a pretty stable radical. After converting himself to his master Liebig's theory, Hofmann starts out on a new line of work. If aniline is a substituted ammonia, says he, why, then, if I treat it with ethyl bromide, I ought to replace one of the hydrogen atoms by ethyl.

Sure enough, by the action of dry aniline upon ethyl bromide, he obtains the so-called imidogen compound predicted by Liebig, and the proof of the substitutability of ammonia hydrogen atoms is made. The substance obtained was the hydrobromate of ethyl-phenyl-amine. Next he substitutes the remaining hydrogen atom of ammonia by producing di-ethyl-phenyl-amine. Hofmann then finally succeeded in adding to this tri-substituted ammonia a molecule of ethyl iodide, and he obtained phenyl triethylammonium iodide, which was quite different from the di- and tri-substitution products. It was metallic in nature and acted like ammonium iodide. On treating it with moist silver oxide he obtained phenyl-triethylammonium hydroxide in crystals, which deliquesced and gave as decomposition products H_2O, C_2H_4 and $C_6H_5(C_2H_5)_2N$. It was basic and caustic, destroying tissue and vegetable colors as readily as caustic potash, and bitter as quinine. Würtz, in 1849, proved the same thing that Hofmann did, but from a different point of view. He made the methyl and ethyl esters of cyanic and cyanuric acids and heated these with water, which yielded him the alkyl-ureas, *i. e.*,

diethyl- and dimethylurea, just as Wöhler had previously obtained urea from cyanic acid. When he then treated these alkyl-ureas or simply the cyanic esters themselves with caustic potash, he obtained the substituted ammonias themselves as strong alkaline limpid liquids:

$$HCNO + 2KOH = K_2CO_3 + NH_3$$
$$CH_3CNO + 2KOH = K_2CO_3 + NH_2CH_3$$
$$C_2H_5CNO + 2KOH = K_2CO_3 + NH_2C_2H_5$$
$$CO\begin{matrix}NH_2\\NH_2\end{matrix} + 2KOH \equiv K_2CO_3 + 2NH_3$$
$$CO\begin{matrix}NH.CH_3\\NH.CH_3\end{matrix} + 2KOH = K_2CO_3 + 2NH_2.CH_3$$
$$CO\begin{matrix}NH.C_2H_5\\NH.C_2H_5\end{matrix} + 2KOH = K_2CO_3 + 2NH_2.C_2H_5$$

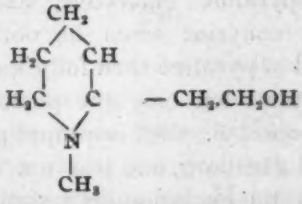
This, then, proved conclusively the nature of the substituted ammonias, and that, in all probability, all alkaloids were ammonia in which one or more of the hydrogen atoms had been replaced by oxygenated or non-oxygenated radicals. The next step in the development of the constitution of the alkaloids was the result of Gerhardt's distillation of quinine, cinchonine and strychnine with caustic potash, whereby he obtained quinoline, and of Anderson's study of the so-called Dippel's oil, an oil obtained from the destructive distillation of animal matter, and also called "Oleum animale Dippelii," which yielded him pyridine, picoline, lutidine and other volatile basic oils, and of bone oil, which yielded the same products. Some chemists now held that possibly alkaloids were not at all derivatives of ammonia, but might be derivatives of some of these newly discovered volatile bases, pyridine, quinoline, etc. It was not until 1867 that these bases were more definitely studied, and the fact established that they were not substituted ammonias, but nitrogenous hydrocarbons, *i. e.*, fundamental substances which could yield innumerable derivatives just as did benzene, anthracene, naphthalene, etc. In 1869 the next step was made by Körner, when he showed that just as naphthalene is made up of two benzene nuclei, so is quinoline made up of a pyridine and a benzene nucleus, *i. e.*, benzene: naphthalene as pyridine: quinoline. Ladenburg, in 1883, proved the correctness of the view by actually converting pyridine into benzene. In 1869 the first "apo" alkaloids were made, *i. e.*, alkaloids obtained from other alkaloids by the abstraction of one molecule of water; thus apomorphine and apocodeine are merely

morphine and codeine minus a molecule of water in each case. Chemists now undertook to decompose alkaloids and obtain decomposition products from them, and from these determine what are the constituent parts that make up the molecule, and, as a final stage, what is the hydrocarbon of which they are derivatives? Thus in 1871, Kraut, in distilling piperine-trichloracetate with silver oxide, noticed that pyridine was eliminated, and at once supposed it was a derivative of pyridine. Later, Hofmann, in 1879, transformed piperidine into dibrom oxy-pyridine by heating it to 220° with bromine and water. Next, Königs succeeded in converting piperidine into pyridine by oxidizing it and removing six hydrogen atoms. This made it appear to be a hexa-hydro-pyridine derivative. He next tried the reverse process, and by reducing pyridine in alcoholic solution with sodium converted it directly into piperidine. This proved that piperidine is hexahydro-pyridine, and we know its constitution. Synthesis now came to the aid of chemists to help unravel the constitution of these complex alkaloids, and, in case of piperine, it was Ladenburg who, in 1885, treated dicyan-trimethylene with sodium in alcoholic solution and obtained, as expected, pentamethylene diamine. On rapidly distilling the latter it is decomposed into free ammonia and piperidine identical with the natural product. What first, however, put confidence in this work of determining alkaloidal constitution was the brilliant work of Ladenburg on atropine, not only because it showed how beautifully the constitution of these substances could be unravelled, but also because it was a generally used substance and the actual identity, both chemically and physiologically, could readily be determined. If atropine could successfully be made synthetically, why could not any alkaloid? Atropine was isolated in 1833 by Geiger and Hesse, and its formula $C_{17}H_{23}NO_3$ was established by analysis by Liebig. It is lævogyre, bitter and powerfully dilates the pupil. Kraut and Lossen, in 1863, showed that atropine was an ester, as barium hydrate will split it up at 60° into tropine and tropic acid:

$$\underset{\text{Atropine.}}{C_{17}H_{23}NO_3} + H_2O = \underset{\text{Tropine.}}{C_8H_{15}NO} + \underset{\text{Tropic Acid.}}{C_9H_{10}O_3}$$

If the reaction is prolonged decomposition proceeds further, and the tropic acid is converted into atropic acid $C_9H_8O_2$ by loss of H_2O, and if the temperature should rise to 180° C. the tropine will also lose a molecule of water and be converted into tropidine $C_8H_{13}N$.

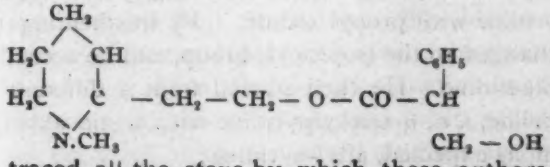
In 1879 Ladenburg heated on a water-bath the salt tropine tropate with dilute hydrochloric acid, and thus artificially produced the opposite reaction to that just given, and the result was the elimination of a molecule of water, and the formation of atropine, which possessed all the physical and physiological properties of the natural alkaloid. Faith in synthesis was established. For establishing this faith Ladenburg has this year, as we have just heard, been decorated by the British Society with the Hanbury Medal, the highest gift pharmacy can bestow upon scientific sages. By varying the acid, Ladenburg made a whole line of so-called tropeines, *i. e.*, he used valerianic, acetic, butyric, salicylic, benzoic, etc., acids and obtained valeryl-tropeine, acetyl-tropeine, etc. Some of these were also found to possess mydriatic properties. The constitution of tropine was worked out by Ladenburg and Merling, and found to be as follows:



i. e., a tri-hydro-pyridyl-ethyl alcohol or derivative of pyridine. The constitution of tropic acid has also been determined by the same author and found to be

$$C_6H_5 - CH < \begin{matrix} CH_2.OH \\ COOH. \end{matrix}$$

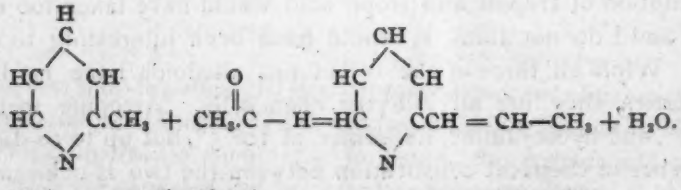
and this has been confirmed by synthesis. This gives us the constitution complete of atropine:



To have traced all the steps by which these authors found the constitution of tropine and tropic acid would have taken too much time, and I do not think it would have been interesting to all of you. While all three of the belladonna alkaloids have mydriatic properties, they are all different chemically. Atropine melts at 115·5°, and hyoscyamine, its isomer, at 108·5°, but up to to-day the difference in chemical constitution between the two is unknown, as hyoscyamine changes into atropine even when it is melted. They are probably stereo-isomers.

Hyoscine, which is identical with scopolamine, however, is different from the other two, atropine and hyoscyamine, as it melts at 59°, and when split up analogously to atropine, yields scopoline and tropic acid, while atropine, as we saw, yields tropine and tropic acid. That scopoline is different from tropine their melting points show, tropine melting at 62° and scopoline at 110°.

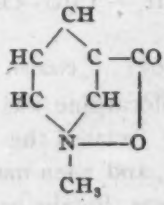
The first alkaloid made synthetically was, however, coniine, because it is such a simple derivative of pyridine, being *α*-propyl-piperidine, *i. e.*, *α*-propyl-hexahydropyridine. This synthesis was also made by Ladenburg in 1885. Before this synthesis, however, the constitution of the alkaloid had been definitely established by Hofmann in 1884. On heating some coniine with some zinc dust, he observed a great evolution of hydrogen, and obtained as a residue the alkaloid conyrine—$C_8H_{17}N = C_8H_{11}N + 6H$. This indicated that it was a pyridine derivative, and Hofmann confirmed this by oxidizing conyrine when he obtained picolinic acid—a monocarbonic acid of pyridine then fully known. The difference in composition by atoms left only the possibility of the side chain being propyl or isopropyl. But isopropyl-pyridine had been made synthetically by Ladenburg, and was not identical with conyrine, hence conyrine is by exclusion propyl-pyridine. Hofmann confirmed this also by reducing coniine by hydriodic acid when he obtained normal octane, which would have been impossible if the coniine had contained an isopropyl group. As coniine was shown to yield conyrine and six hydrogen atoms by reduction with zinc dust, it follows that coniine is propyl-hexahydro-pyridine, *i. e.*, propyl-piperidine. Ladenburg tried to make the synthesis of coniine by heating pyridine with propyl iodide. By this heating the propyl group is changed to the isopropyl group, and he actually obtained isopropyl-piperidine. He then started from a different source by heating picoline, *i. e.*, *α*-methylpyridine with acetic aldehyde, which yielded him, as expected, allyl-pyridine:



Picoline. **Acetic Aldehyde.** **Allyl-pyridine.**

Upon merely reducing this allyl-pyridine eight hydrogen atoms were added, and the result was coniine. It was an ingenious idea, very simple, but very ably executed.

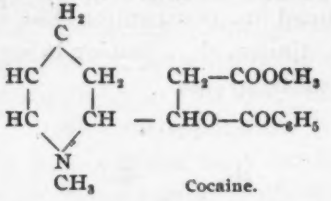
The next alkaloid to be made synthetically was trigonelline, the alkaloid of *Trigonella fœnum-græcum*, commonly called fœnugreek seed. It was first obtained by Jahns, in 1885, and in the succeeding year he determined its constitution, finding that it was the methyl betaine of nicotinic acid; a betaine being an inner anhydride of an acid and an alkaline group.



This he was enabled to do as the result of the studies Hantzsch was just at the time making of the betaines of pyridine carbonic acids, and in particular made them of both nicotinic and picolinic acids. Both were of course isomeric with one another, and both were isomeric with trigonelline, but Hantzsch failed to discover by a comparison that the latter was identical with one of them. Jahns was just working on trigonelline, and on comparing it with both of them, found that it was identical with that of nicotinic acid, which is β-pyridine carbonic acid.

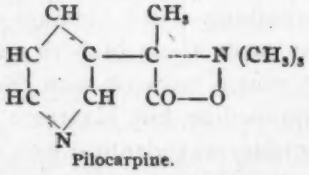
The great step in the advancement of alkaloidal constitution was the complete and thorough study made in the eighties of pyridine and quinoline and their derivatives. By obtaining nearly all the derivatives of these two substances investigators were able, in studying and breaking down alkaloids by oxidation or reduction, to gain a definite foothold, so to speak, and grasp something that they knew the composition of, and would aid them in their further work and conclusions. The great development of synthetic methods also helped along this work and especially served to confirm work that had been more or less problematical before. Among the opium alkaloids, those that were known constitutionally at about this period, in 1886, are narcotine and papaverine, the former being a very complex pyridine and the latter a quinoline derivative, the former being the combined work of Matthiessen, Wegscheider and Roser

and the latter of Goldschmidt. Cocaine was isolated by Niemann, in 1860, and its formula determined by Lossen, but Einhorn first, in 1888, determined that it was an ester, *i. e.*, methyl-benzoyl ecgonine, and further determined that ecgonine was methyl-tetrahydro-pyridyl-β-oxypropionic acid, and that hence cocaine is the methyl ester of methyl-tetrahydro-pyridyl-β-benzoyl-propionic acid.



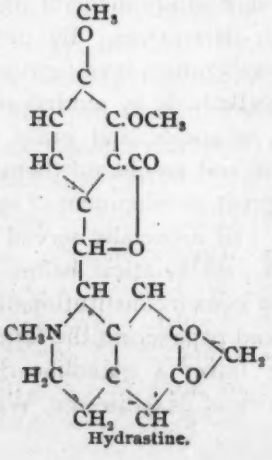
Cocaine.

At about this time also pilocarpine was being studied by Hardy, in Paris, he also first having isolated the alkaloid in 1874, and he worked out the constitution, and then made a successful synthesis of the same. He found it was Betain or inner salt of β-pyridine lactic acid.



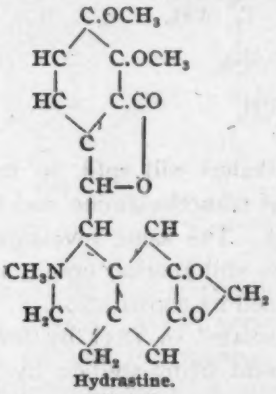
Pilocarpine.

In 1890 the constitution of hydrastine was worked out by Freund and Phillips, who were aided in their work by the fact that Roser had not long previously worked out the constitution of the very similar alkaloid narcotine. This is an iso-quinoline derivative.

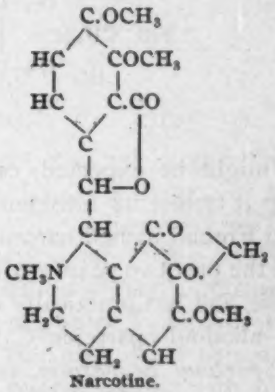


Hydrastine.

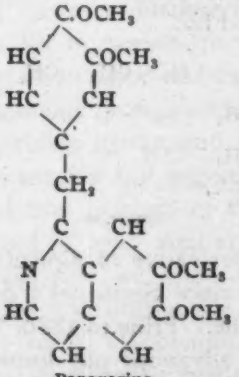
It is very interesting to observe the very close similarity between the three alkaloids, narcotine, papaverine and hydrastine, constitutionally speaking, and I imagine that a closer comparative pharmacological study of these three in connection with one another would prove of interest, for it certainly seems more than likely that three substances that are so closely allied, atomically speaking, should possess very similar physiological properties:



Hydrastine.
$C_{21}H_{21}NO_6$

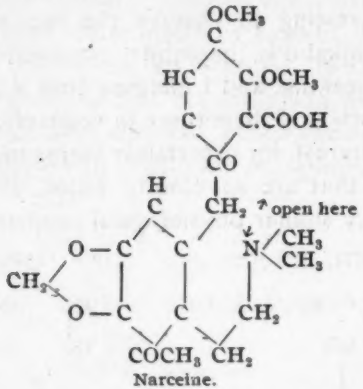


Narcotine.
$C_{22}H_{23}NO_7$



Papaverine.
$C_{20}H_{21}NO_4$

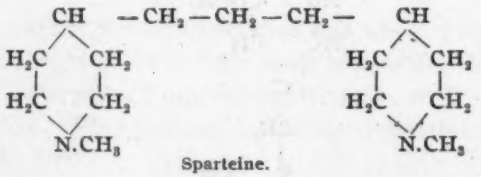
According to Freund, narceine, another opium alkaloid $C_{23}H_{27}NO_8$, is closely related to narcotine chemically, and all his results and work, covering a period of a year or more, point to the fact that it is not an isoquinoline derivative, but that the nitrogen is part of an open chain. This would account for its unusually weak alkaline reaction, for its salts are not stable, and its alkalinity is very unpronounced.



Narceine.

As might be expected, caustic alkalies will split up narceine, causing it to lose its nitrogen atom as trimethylamine and forming an acid Freund named narceonic acid. The same investigator has also in the past two years worked upon still another opium alkaloid, thebaine, and has practically determined its constitution.

The alkaloid sparteine $C_{15}H_{26}N_2$, isolated in 1851 by Stenhouse from *Spartium Scoparium*, is at present being studied by Ahrens, and he feels reasonably sure that the composition of its tetrahydro derivative is represented by

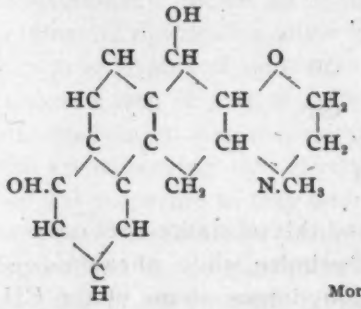


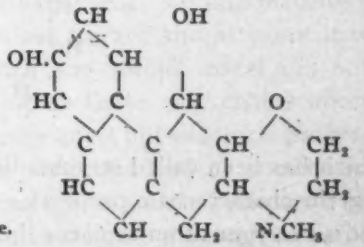
Sparteine.

and that it is hence a derivative of dipicolylmethane.

Many investigators since Sertürner's day have worked on the constitution of morphine. Prior to 1889, Von Gerichten, Schrötter and Otto Fischer had advanced our knowledge very much, but it was not until the discoverer of antipyrine (Knorr) published his first papers on the subject that definite knowledge could be said to have been established. The number of derivatives of morphine that have seen the light of day during these twenty years runs up into the hundreds, and the end is not yet. When the day comes that Von Gerichten and Knorr can agree to the arbitration of their respective cases, the accumulation of morpholines, morphomethines, etc., will probably cease, but not until then. Pending this day, the

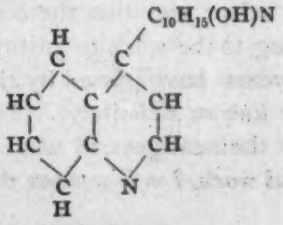
formula of Knorr is usually accepted as very near the truth, and as such we will accept it. It is a morpholine derivative of the hydrocarbon phenanthrene, and the questions remaining open are at which of two of the three benzene rings of phenanthrene the morpholine ring is attached, and (2) exactly where the two hydroxyls are located. I will give you both, and you can have your choice:



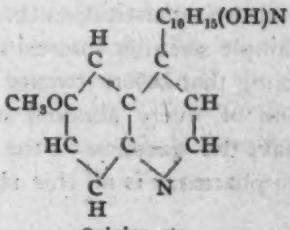


Morphine.

There can be no doubt that this question of final doubt will ere long be settled. What was said of morphine is equally true of quinine, for one investigator of the constitution of this alkaloid alone, Königs, could fill a good-sized quarto volume with his own work. The question is, however, further removed from solution than in case of morphine, for in case of quinine there is an entire group, $C_{10}H_{15}(OH)N$, that is more or less a mystery. On the face of it, it appears like a quinoline group, but it has been settled that it is not, but rather a pyridine group, and tetra-hydrated at that, and somewhat similar to tropine and ecgonine. The fact that cincholoiponic acid, an oxidation product of cinchonine, is both isomeric with tropic acid and of very similar constitution, indicates this very strongly. At any rate, we know that quinine, quinidine and quinicine are identical constitutionally, but are stereochemic isomers, and the same is true of cinchonine, cinchonidine and cinchonicine. The difference between the two groups is one methoxyl group, OCH_3, as the formulas below indicate:

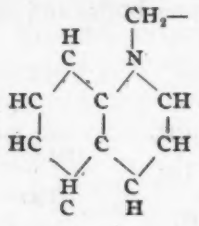


Cinchonine, etc.

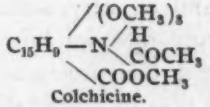


Quinine, etc.

Of strychnine we know that it is a quinoline derivative, as Gerhardt, way back in the forties, obtained quinoline from it. While many have worked upon strychnine, the main work that bears upon its constitution has been done by Tafel. This work has shown that it is a derivative of a nucleus of formula



which has been called strychnoline, and this substance does not possess the characteristic properties of strychnine, while, when oxidized and an oxygen atom replaces the two hydrogen atoms of the CH_2 group, it assumes the poisonous and cramp-producing properties of strychnine. Just how the remaining part of the strychnine molecule is made up is at present unknown. Colchicine has been studied by Zeisel for some years and he has ascertained that colchicine is the methylester of colchiceine and that the latter contains a carboxyl group COOH. He has made numerous derivatives of colchicine and has established that it is not a pyridine or a quinoline derivative, but that the nitrogen is in all probability present in the form of an acetylated amido group. An atomic group $C_{15}H_9$ is as yet undetermined in case of this alkaloid and, as far as known, the constitution is supposed by Zeisel to be



Colchicine.

I have now brought the constitution of the alkaloids up to date, and we have observed that at the present day more work is being done on their constitution than ever before, and that there appears to be ample scientific interest attaching to the work to justify me in predicting that before twenty more years have passed by the constitution of every alkaloid will be known definitely. To those that have the question on the tips of their tongues, of what advantage to pharmacy is all this structural work, I will answer that it is

of manifest advantage to both pharmacy and chemistry. To chemistry because it marks in each case, as a fact established, a milestone for the guidance of subsequent workers, and chronicles the existence of another truth; to pharmacy, because its advent means another step toward possibly improved medicaments, not to mention possibly greatly cheapened drugs. When morphine, for instance, shall be constitutionally known, its synthesis from phenanthrene is within the range of probability, and with this comes the ultimate reduction of its price to that of quinine, or, perhaps, less. To pharmacology it means a step in case of each alkaloid toward the attainment of ideal medication, *i. e.*, medication with one specific effect and not with accompanying side effects. Just as these side chains affect chemical properties so they undoubtedly affect physiological properties, and if morphine, for instance, is a narcotic and an anesthetic, and, perhaps, has certain deleterious influences on the brain centres, the lining of the stomach, kidneys, etc., that we may call bad side effects, and that are unfavorable to the use of the drug, there is a possibility opened to view of so removing some of these chains or groups and adding others as to make of morphine an anesthetic without any narcotic effects or without those brain and stomach effects that now render it the curse of many a family. That this is possible, nay, more, that it will be the natural development of medicine and pharmacology in the next century, I am prepared to positively assert. It will come as sure as the sun rises in the east and sets in the west, for the whole trend of advanced medical thought is in that direction, and when it does come it will come as the result of just such study as I have been endeavoring, I hope with some measure of success, to lay before you this evening.

ALGÆ AS A CAUSE OF THE CONTAMINATION OF DRINKING WATER.

By G. T. Moore.

The widespread interest which has been aroused throughout the country within the last ten years with regard to the securing of sanitary water supplies is evidence of the importance of the problem, and no effort is now considered too great or too costly that will insure to the public a constantly pure and wholesome flow of this most necessary article.

The question is one which naturally appeals to the engineer, and for a long time it was left entirely to him to determine not only how the water was to be obtained and supplied, but also its quality. Too often the quality was a matter that was given little or no consideration, and topographical or financial consideration decided in favor of a supply that afterwards proved to be unfit for use, if not absolutely dangerous. Later, the chemist was called in, and, while people now knew just the amount of mineral and organic matter contained in the water and deductions could be made showing that this matter probably came from certain sources, there was still no getting at the actual cause of a great deal that contaminated water supplies until recourse was had to the microscope. It is quite as necessary to determine the origin and condition of organic matter found in water as to know the exact quantity and quality of it, and in many cases the true interpretation of a chemical analysis depends entirely upon a direct biological examination.

The history of the microscopical study of water in connection with its wholesomeness is one which extends over a comparatively short time and, until quite recently, there have been scarcely any who gave their whole attention to this aspect of the subject. It is, however, fast becoming recognized as most important and necessary, and the public are coming to demand that the water they use be subjected to biological examination as well as chemical analysis.

It will, perhaps, be profitable to consider a few special forms which give rise to disturbances in water supplies, and to point out some of the reasons for these organisms causing pollution and unwholesomeness.

We shall confine ourselves to a group of plants known as the algæ, which, aside from the bacteria, produce more trouble than any other members of the vegetable kingdom. The bacteria are recognized as being responsible for much disease and discomfort, although the actual number which prevent the same is vastly in the majority. This group and certain animals of a low order which contaminate water would each form the subject of an entire article, and for this reason, must be left out of consideration at this time.

The group of the algæ contains a number of forms which are wonderfully varied, both as to their size and method of growth; and, while the large red and brown "sea-weeds" belong to this class, it is the grass-green forms which are most often found in fresh water.

Certain of this latter kind can frequently be observed in quiet or stagnant pools, and are popularly termed "pond scum," "frog spawn," etc. It is not to these easily-discerned plants, however, to which we usually have to look for the cause of the pollution of most water; while they may cause considerable damage and trouble in a mechanical way, and it is generally the desire of the engineer to keep them out of his reservoir, they are probably a benefit rather than a detriment so long as they are in active, healthy condition. It has been found that volatile, fatty acids, such as butyric and valerianic, together with glucose, leucin, tyrosin and even urea, when properly diluted, can be assimilated by such plants, and no doubt a considerable number of organic substances which are carried into rivers by drains are destroyed by the larger green algæ and diatoms. It must be remembered, however, that a good share of this work is accomplished by the so-called "water bacteria," which are everywhere present.

The group of plants which is, perhaps, best known as polluting drinking water is the one containing the forms popularly called the "blue-green algæ." Whether, in the technical sense, they really are algæ is, perhaps, a question, as they are much simpler in structure than the true algæ, and show a great resemblance to the bacteria, both vegetatively and in their methods of reproduction. This is so evident that the blue-green forms have been put with the bacteria into a separate group known as the SCHIZOPHYTA, and termed *Schizophyceæ*, while the name *Schizomycetes* has been applied to the bacteria. As the common name denotes, these plants are usually of a bluish-green color, but this is not universally true, for they may assume various shades of olive, yellow and brown, even appearing chocolate or purplish-red at times. The blue-green shades are brought about mostly by various mixtures of "leaf-green," or chlorophyll, with a substance of a nitrogenous or proteid nature, known as phycocyanin. Sometimes there is a coloring matter in the gelatinous sheath of the plant called scytonemin, which is responsible for the reddish, violet and brown shades, but in addition to this it seems possible that a few forms contain numerous gas vacuoles, which line the inner walls of the cells, producing an optical effect which makes them appear red or chocolate. This is probably the cause of the color of *Trichodesmium erythræum*, which gives the name to the Red Sea, and of certain oscillatorias in this country which cause ponds and pools to become a deep chocolate brown.

Structurally, the Schizophyceæ are very simple indeed. Many of them consist of but a single cell, and multiply by merely dividing and giving rise to two cells like the parent. Others are composed of a series or chain of cells which are held together by a gelatinous envelope, or there may be direct protoplasmic communication between the cells. The contents, however, vary but little with the external appearance of the forms. While the cells are filled with protoplasm and have the usual granules, vacuoles, etc., it is extremely doubtful whether or not there is a true nucleus. The coloring matter, instead of being confined to definite bodies, as in the true algæ, is distributed throughout the cell contents or forms a sheath lining the wall of the cell.

In addition to the simple method of division, certain groups of the Schizophyceæ have the power of forming thick-walled spores, and it is by means of these cells that they are able to tide themselves over adverse conditions which it would be impossible for their vegetative cells to withstand. Thus it is that a form which has once existed in a pond or stream may disappear for several years, and then suddenly make its appearance, because the spores made by the plants in the first place, having remained in the mud at the bottom, reach maturity, and the combination of temperature, nutrition, etc., are favorable for germination. The conditions most favorable for the rapid increase of the blue-green forms are shallow, stagnant water and relatively high temperature. Consequently it is during the summer months that the most trouble and annoyance is experienced from these forms. The well-known "pig-pen" and "grassy" odors are given off and water supplies rendered quite unfit for use by the unpleasant odor and taste. Jackson and Ellms have shown that these odors are due to the breaking down of highly organized compounds of sulphur and phosphorus, and to the unusually large amount of nitrogen which these plants contain.

As usually classified by botanists, the Schizophyceæ are divided into two groups, the Coccogoneæ and Hormogoneæ, according to whether the plant consists of a single cell or a number of cells. The Hormogoneæ are further distinguished by the power they possess of breaking their filaments up into smaller groups of cells called hormogonia, which may divide rapidly and give rise to new plants. The only genera among the unicellular group which are likely to cause trouble are *Cœlosphærium* and *Clathrocystis.* These are quite

similar in general appearance, consisting of a gelatinous mass in which are embedded bluish-green cells of either spherical or oblong shape. There is no connection between the cells, and the colonies are capable of being broken up into smaller groups, each cell of which divides rapidly, and thus new masses are formed. In *Clathrocystis* the colony sends out buds or projections which soon fall off, and these grow into new colonies like the original one. Among the Hormogoneæ there are quite a number of genera which have been reported to be the cause of various odors and tastes in drinking water. The members of the nostoc tribe are particularly obnoxious, and, since all can produce thick-walled spores in addition to their vegetative method of propagation, it is often a most difficult matter, after they once make their appearance, to get rid of them.

The following key will give some idea of the various forms of Schizophyceæ which have been found to contaminate the water in which they occur, and will bring out the morphological points which are depended upon for their determination.

SCHIZOPHYCEÆ.

(*A*) Plants consisting of a single cell, occasionally united into colonies by being embedded in a gelatinous matrix.—I. Coccogoneæ.

(*B*) Plants always of more than one cell, forming simple or branched filaments, which may or may not be enclosed in an outer gelatinous layer or sheath.—II. Hormogoneæ.

(*I*) Coccogoneæ.

(*1*) Cells free or only slightly held together, not forming a definite colony.—*Chroococcus.*

(*2*) Cells held together in a gelatinous matrix and forming colonies of regular outline.

(*a*) Colonies at first solid, several rows of cells thick, becoming saccate and perforated.—*Clathrocystis.*

(*b*) Colonies hollow, cells only on outer surface.—*Cœlosphærium.*

(*II*) Hormogoneæ.

(*1*) Cells generally differentiated into three kinds: (1) vegetative cells; (2) spores, and (3) heterocysts. The latter usually being of different color, clearer contents, and

with thickenings in the walls adjoining the vegetative cells or spores.—(*a*) Heterocysteæ.

(*2*) Cells in each filament undifferentiated. No heterocysts.—(*b*) Homocysteæ.

(*a*) Heterocysteæ.

† Filaments irregularly interwoven and contorted, enclosed in a definite gelatinous mass.—*Nostoc.*

†† Filaments free or but slightly united.

ϕ Heterocysts and spores intercalary.

* Filaments free or united in a formless mass —*Anabaena.*

** Filaments densely agglutinated in fascicles often of considerable size.—*Aphanizomenon.*

$\phi\phi$ Heterocysts and terminal spores contiguous.—*Cylindrospermum.*

(*b*) Homocysteæ.

† Filaments simple, with an evident sheath.—*Lyngbya.*

†† Filaments simple, sheath wanting or very slight, plants possessing a characteristic movement.—*Oscillatoria.*

Another great group of plants which of late years has been shown to be of importance in the consideration of the biology of drinking water is that known as the Diatomaceæ. By some botanists these forms are believed to be closely related to the Desmids, an order of the grass-green algæ, which seems to resemble them in certain points of morphology and reproduction. On the other hand, there are those who maintain that the diatoms are a special class, being much older than the desmids, and that the points of resemblance are only analogous, not homologous, it therefore being impossible to regard them as proofs of genetic relationship. Whatever their affinity with other algæ may be, they certainly constitute the largest group of any of the aquatic plants, there having been more species of diatoms described than all of the red, brown and green algæ taken together. It is probable that a great many of these species are not good, but even after making full allowance for such duplication there still remains an enormous number of separate and distinct forms.

In structure, a diatom is not unlike a minute glass box, for it is made up of two halves, one fitting tightly within the other, and having its walls strongly silicified. It is this silica which makes the diatomaceous earth valuable for polishing powders. In at least one article on the market diatom shells form a considerable part of a tooth powder, and the bad effect of such hard material on the teeth is so obvious that it would be well for every one to have a microscopical examination made of any powder to be used in this way. Earth containing the remnants of diatoms is also used extensively in the manufacture of dynamite, and the living marine forms constitute a valuable part of the food of some fishes.

These plants have a peculiar method of vegetative multiplication which is unlike anything found elsewhere among the algæ. The two halves of the "box," which are called valves, begin to separate slightly from each other, and as the contents divides into two parts, there is formed within two new halves, one fitting into the larger half of the original cell, and the other forming a new box with the smaller half of the parent plant. These then separate, and thus there are formed two diatoms of exactly the same construction as the mother cell, although one is a trifle smaller than the other. In addition to this method of propagating the species, there are various ways by which the plant forms a single large resting spore; and recently it has been discovered (chiefly through the work of Castracane and Murray) that it is probable that the whole contents of a diatom cell may break up into a number of small spores, each one of which develops into a new plant.

There are only a few species which are known to give rise to serious trouble in water supplies, but these occur quite frequently and in great quantities. Usually the infected water has an aromatic odor, variously described as resembling fish or geraniums, and the taste is disagreeable enough to render it quite unfit for use. In addition to this effect, however, diatoms are extremely troublesome when contained in water to be used for the manufacture of paper or for laundry purposes, because of the greenish-brown coloring matter they contain, and which stains articles coming in contact with it. Whipple has observed that the growth of diatoms seems to depend upon certain definite conditions of the water; that is, they do not develop when the bottom of the pond or reservoir is quiet, but in spring and fall, when the rising or lowering temperature

causes the water to circulate and a good supply of air and nitrates is obtained, the growth is most luxuriant. Thus it is seen that temperature is only an indirect cause, and not one that need be taken into account by itself.

The class Syngeneticeæ comprises a number of organisms which until recently have been considered animals. Some of them are certainly plants according to present-day standards, and others are so near the line separating the two kingdoms, that botanists are beginning to study these forms quite as much as zoölogists. There is a single member of this class which probably causes more trouble in water supplies than any other organism, either plant or animal.

This form, known as *Uroglena*, is frequently found in New England, and has been reported as far west as Indiana. The probabilities are that it is widely distributed in this country, but has not yet been recognized in many localities. In appearance *Uroglena* resembles a colorless sphere with numerous small greenish cells embedded in its periphery. The whole colony may become almost a half millimetre in diameter, although it is usually much smaller. The individual cells are each provided with a pair of cilia of unequal length, and it is by the vibration of these that the whole colony is revolved through the water. Each cell of the colony contains a nucleus, a red spot and a single greenish color body, besides several vacuoles. In addition, there is a considerable number of oil-globules, and it is the liberation of this oil which causes the fishy, oily taste and odor produced by *Uroglena*. Among the algæ and Schizophyceæ the contamination is nearly always brought about by decay, but in this case the trouble is produced simply through the mechanical breaking up of the organism and the consequent liberation of the oil contained within the cells. Usually the pumping or gravity necessary to distribute the water is sufficient to free the oil, for the cells are very fragile. In one instance, where the water was used almost continuously for several days for washing caterpillars off the trees, a marked increase in the disagreeable odor and taste was the result. The exact nature of this oil is not very well understood. Calkins, who isolated and concentrated it, believed it to be similar to the essential oils. It was non-volatile at the temperature of boiling water, and seemed to resemble the oils obtained from diatoms and the blue-green forms.

No sexual method of reproduction has as yet been observed

in *Uroglena*, but it has a rather peculiar method of cell division which enables it to multiply rapidly. Before a cell divides it turns in the periphery of the hollow gelatinous sphere, until it is in a position at right angles to the one usually occupied. Then at the end of the cell which originally pointed towards the centre of the sphere there are formed a pair of cilia like those at the opposite pole, and a red spot appears. The cell then begins to be sharply constricted, and as it gradually divides the two halves are drawn back through an angle of 45°, so that when the new cells are finally formed they occupy a position similar to the one normally held by the mother cell. When a colony becomes too large it breaks up into individual cells, and these soon, by repeated division, grow into new spheres. In addition to this way of multiplying, resting spores are formed, which enables the organism to survive conditions which would otherwise exterminate it. In this country, *Uroglena* seems to thrive best in cold temperatures, it usually occurring in greatest numbers when the water is frozen over. Just the reverse is true in Europe, where it is most abundant during July and August, and disappearing entirely at the approach of cold weather. For a number of reasons it seems probable that the European form is quite a different species from the one which causes so much trouble in America.

There are others of the Syngeneticeæ which contaminate water, although not to the extent that *Uroglena* does. *Synura* and *Syncrypta* are both known to have a bad effect, *Synura* being responsible for the "ripe cucumber" odor which was formerly thought to be caused by fresh-water sponges. It is probable that these two forms are really the same thing, and Dr. Kirchner, in a note to Hansgirg, has said that he united the two under *Synura*, as he did not consider that a true generic difference existed between them. The somewhat uncertain genus *Uvella* should perhaps be mentioned here. This form, which greatly resembles *Synura*, has been reported as being one to be most dreaded, causing an exceedingly disagreeable taste that was almost acid. Whether this organism really has this effect has been questioned, but it ought to be watched for and further investigations made.

Enough plants have been referred to to make it evident that in dealing with such a variety of forms having such varied methods of growth and reproduction, it would be quite impossible to have any

single remedy that would prevent or remove all the unpleasant effects caused by these organisms. Each form must be studied by itself, and it is only after all the information possible has been obtained with regard to its life history and conditions necessary for growth that we can hope to prevent or exterminate it. Large quantities of statistics are available, showing the kind and extent of the organisms most likely to occur in water supplies, and we have some little information with regard to the climatic conditions which are most conducive to their rapid growth; but there is still wanting a great many details which can only be obtained from patiently cultivating these plants in the laboratory. On the other hand, certain general precautions can be taken, such as removing the top soil in making new reservoirs and storing ground water in the dark, which undoubtedly prevents the introduction and growth of many of the most troublesome forms, and wherever it has been possible to apply these methods the result has justified the expense. It is certain that it is just as necessary to have a thorough microscopical examination of a water supply as it is to have a chemical analysis, and usually the most practical application of the knowledge thus obtained can be made. In some cases, where the cause of pollution has been shown to be due to some plant living in the water, it has been possible to cut out that part of the supply until after the cause has disappeared. Again, the immediate detection of obnoxious forms often permits of their removal before decay and pollution take place. As soon as people understand that something more than a mere analysis by a chemist or an inoculation of guinea-pigs is necessary before the purity of a water supply can be ascertained, there will be a greater demand for those who can make accurate microscopical examinations, and we may hope for an increase in our knowledge of this most important aspect of a most important subject.

Direct references to the literature were impracticable throughout the foregoing, but a short bibliography is appended for the benefit of those who may wish to get more specific knowledge of the points referred to.

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DARTMOUTH COLLEGE.

A NOTE ON THE ASSAY OF OPIUM.

BY WILLIAM R. LAMAR.

Recently the writer, while engaged in assaying a sample of powdered opium, according to the U.S.P. method, noticed, after having exhausted the opium and concentrated these aqueous liquids to 14 grammes; and after its transferrence to a tared Erlenmeyer flask, the weight then brought up to 20 grammes, with the rinsings of the capsule, had been accomplished, that the addition of the prescribed 10 grammes of alcohol caused a very pronounced flocculent precipitate.

This precipitate, after the addition of 25 c.c. of ether, shaking actively, and allowing to stand for a few minutes, did not appreciably diminish.

At the time, it was considered quite likely that the solution of this deposited matter, upon the further addition of the ammonia water, might not be effected, and would therefore contaminate the precipitate, to be subsequently weighed as morphine.

This in reality seems to be the case, as shown by the weight of the crude morphine, and of the matter insoluble in lime water.

It was believed that by increasing the amount of the alcohol, all of this objectionable matter in solution could be gotten rid of prior to the precipitation of the morphine.

With this end in view, a series of experiments was instituted, which resulted in the confirmation of this view, as will be seen from the analytical data to follow.

As the result of his experiments, the writer, therefore, recommends the following modification of the U.S.P. process:

"Introduce the opium (which, if fresh, should be in very small pieces, and if dry, in very fine powder) into a bottle having a capacity of about 300 c.c., add 100 c.c. of water, cork it well, and agitate frequently during twelve hours.

"Then pour the whole as evenly as possible upon a wetted filter having a diameter of 12 centimetres, and, when the liquid has drained off, wash the residue with water, carefully dropped upon the edges of the filter and the contents, until 150 c.c. of filtrate are obtained.

"Then carefully transfer the moist opium back to the bottle by means of a spatula, add 50 c.c. of water, agitate thoroughly and repeatedly during fifteen minutes, and return the whole to the filter.

"When the liquid has drained off, wash the residue, as before, until the second filtrate measures 150 c.c., and finally collect about 20 c.c. more of a third filtrate.

"Evaporate in a tared capsule, first, the second filtrate to a small volume, then add the first filtrate, rinsing the vessel with the third filtrate, and continue the evaporation until the residue weighs 14 grammes.

"Rotate the concentrated solution about in the capsule until the rings of extract are redissolved, pour the liquid into a tared Erlenmeyer flask having a capacity of about 100 c.c. (here it will be best to employ a flask of about 150 c.c. capacity), and rinse the capsule with a few drops of water at a time, until the entire solution weighs 20 grammes."

Add 60 grammes (73·2 c.c.) of alcohol, cork well, and shake actively for one minute, allow the flask and contents to stand for thirty minutes undisturbed, when the precipitated matter will have completely settled.

Now carefully decant the clear supernatant liquid into a tared capsule, transfer as much as possible of the precipitate to a filter of 7 centimetres diameter, previously moistened with a mixture of alcohol 3 parts, and water 1 part, by weight, allow the liquid to drain thoroughly, receiving the filtrate in the capsule containing the decanted portion, rinse the flask with small portions of the above alcohol-water mixture until freed from the precipitate, using 2 or 3 c.c. at a time, transferring these to the filter in such a manner as to wash the filter and its contents, and allow to drain before adding the subsequent rinsings.

Then continue the washing of the precipitate and filter, by care-

fully dropping upon the edges of the filter and contents, until the filtrate ceases to possess a bitter taste.

(The filtrate, although free from bitterness, will generally possess a faint straw-yellow color, due to the slight solubility of the precipitate in the washing mixture. This washing can generally be accomplished, by careful manipulation, with 15 c.c. of liquid; in no case, however, is it necessary for the total washings to exceed 25 c.c.)

Add 35 c.c. of water to the contents of the capsule, and having placed same on the water-bath, evaporate until the alcohol has been completely dissipated and the residue weighs 14 grammes, then proceed according to the U.S.P. method.

This additional step in the process can easily be executed in an hour's time, and certainly the purity of the morphine so obtained warrants its future employment.

It will be seen that a correction by any of the commonly used methods is entirely unnecessary.

The following table gives the results obtained by this modification, up to the present time, and the quantity and quality of the morphine obtained by a strict adherence to the U.S.P. method is appended for the sake of comparison.

The results here recorded represent the average of closely-agreeing duplicate assays.

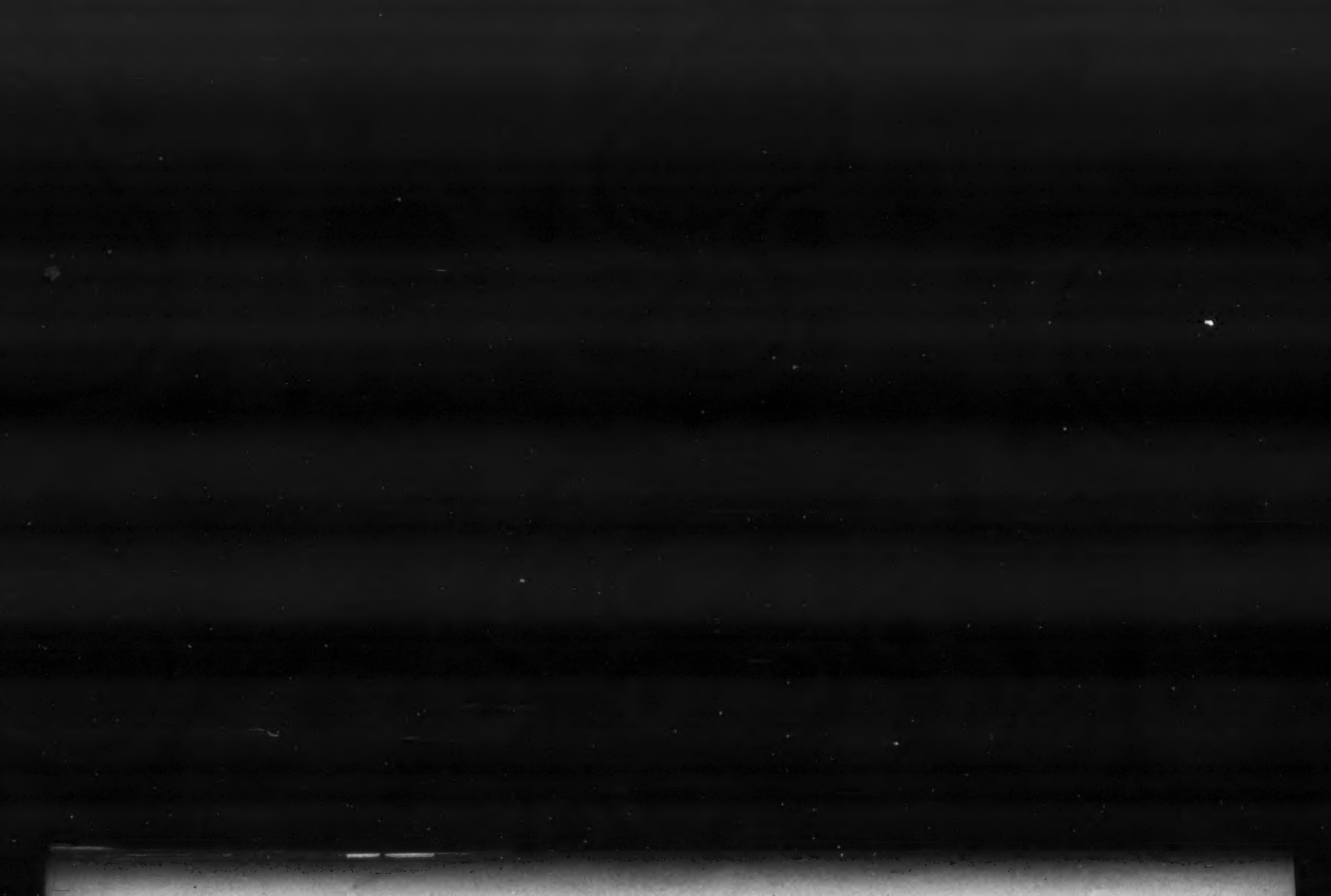
The acid employed in the titrations of the different samples of morphine was a $\frac{N}{20}$ H_2SO_4, which was standardized against sodium carbonate prepared from a specially purified $NaHCO_3$, methyl orange, litmus and phenolphtalein being used as indicators.

The mean of the above results, together with two determinations, according to the method of Weinig, was accepted as the standard.

This acid was employed in titrating crystallized morphine, prepared by precipitation of a saturated solution of its sulphate with a slight excess of potassium hydrate solution, washing until free from sulphates, and from potassium spectroscopically, carefully drying on porous plate, at a temperature of 40°–50° C., then well washing with ether and again drying to a constant weight at the above-mentioned temperature.

The following results were obtained:

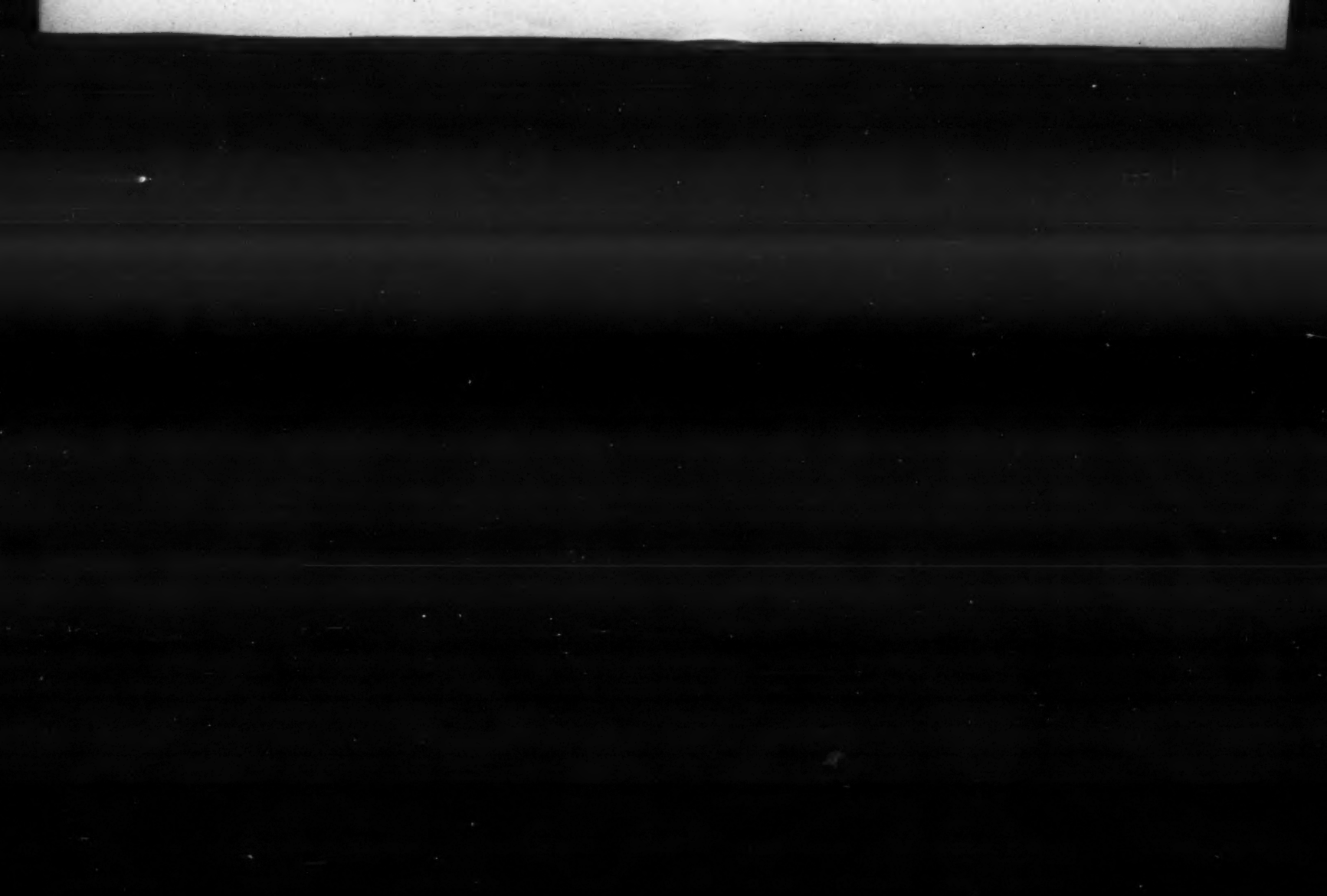
0·220 gramme of morphine required 14·65 c.c. of $\frac{N}{20}$ H_2SO_4. V.S.,



Number and Kind of Opium.	Percentage of Moisture at 100° C.	Time Allowed for Precipitation of Morphine.	Percentage of Crude Morphine Weighed.				Original Weight of Filters.		Weight of Filters After the Detachment of Morphine.		Percentage of Pure Morphine in Opium as Indicated by Lime Water Test.		Percentage of Crude Morphine Insoluble in Lime Water.		Percentage of Pure Morphine in Opium According to Ash Method.		Percentage of Ash in Crude Morphine.		Percentage of Pure Morphine in Opium by Titration with Volumetric Acid.		Percentage of Pure Morphine in Crude Morphine by Titration with Volumetric Acid.		Percentage of Pure Morphine in Crude Morphine by Lime Water Test.		Percentage of Pure Morphine in Crude Morphine by Ash Method.	
			On Filters.		Detached.																					
			U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.	U.S.P. Process.	Modified Process.
1. Powdered,	6·23	16 hrs.	13·52	12·81	13·40	12·78	0·230 gm. 0·2254 "	0·219 gm. 0·2006 "	0·242 gm. 0·2384 "	0·2216 gm. 0·205 "	12·87	12·77	3·92	0·08	12·92	12·73	1·38	0·15	13·21[1] 12·56[2]	12·67	98·64[1] 93·76[2]	99·14	96·08	99·92	96·47	99·62
2. Gum . . .	23·9	15 "	—	—	11·59	11·29	—	—	—	—	11·06	11·29	4·57	0·00	10·75	11·21	2·81	0·27	11·85	11·28	102·26	99·93	95·43	100·	92·81	99·31
3. " . . .	24·7	15 "	—	—	—	9·26	—	—	—	—	—	9·26	—	0·00	—	—	—	—	—	—	—	—	—	—	—	—
4. " . . .	22·8	15 "	—	—	—	9·83	—	—	—	—	—	9·83	—	0·00	—	—	—	—	—	—	—	—	—	—	—	—
5. Powdered,	3·54	15 "	—	—	—	12·58	—	—	—	—	—	12·58	—	0·00	—	12·49	—	0·303	—	12·59	—	100·1	—	100·	—	99·33

[1] Before correction was applied.

[2] After applying correction.



for neutralization = 99·76 per cent., each cubic centimetre of the acid, being the equivalent of 0·015117 gramme crystallized morphine.

0 3292 gramme of morphine required 21·7 c.c. of $\frac{N}{20}$ H_2SO_4 V.S., = 99 64 per cent.

The following mode of procedure was adopted in the titrations. Weigh into a tared beaker between 0·2–0·3 gramme of the morphine, and carefully run in upon it 25 c.c. of $\frac{N}{20}$ H_2SO_4 V.S., stir gently until solution is completely effected, which is quickly accomplished. Add 5 drops of the U.S.P. test solution of cochineal and then run in $\frac{N}{20}$ KOH, V.S., until a distinct pink color appears.

The morphine from Nos. 3 and 4 was destroyed before it was decided to titrate the different samples.

It will be seen from the accompanying table that trustworthy results cannot be secured by titration of the morphine as obtained by U.S.P. process.

This may be explained by the fact that there is present in the morphine an acid-consuming body of a lower molecular weight, at least such seems to be the case with No. 1.

0·3108 gramme of this sample, treated with 10 c.c. of water, transferred to a filter and carefully washed until the filtrate measured 36 c.c., required 1·55 c.c. of $\frac{N}{20}$ H_2SO_4 V.S.

As the solubility of crystallized morphine in water at 15° C. is given at one part in 4,350 parts (U.S.P.), and assuming that the water (36 c.c.) weighed 36 grammes, an amount of morphine (0·0082 gramme) should be in solution, corresponding to 0·55 c.c. $\frac{N}{20}$ H_2SO_4 instead of 1·55 as actually obtained.

Since the above observation was made and the work incidental to it had been completed, the writer's attention was drawn to the fact that a similar observation had been recorded by Mr. L. F. Kebler,[1] but no attempt was made to obviate this difficulty.

In conclusion, the writer wishes to say that a more extended trial will be given the method and the results reported upon in the near future.

Laboratory of Schieffelin & Co., New York.

[1] 1895. *Jour. Soc. Chem. Ind.*, *14*, 464.

RECENT LITERATURE RELATING TO PHARMACY.

KANGAROO TENDONS.[1]

Among the specimens recently received by the Philadelphia Commercial Museum are some kangaroo tendons sent by a surgeon in Australia. The tendons were taken from the tail of the kangaroo, and are preserved in preservative liquid. They are described as being aseptic and chromicized, and are intended for the use of surgeons in sewing up wounds. It is claimed that for this purpose they are superior to the silk threads commonly used. They are said to be strong and to permit of splitting lengthwise to any required fineness without any fraying. Among the specimens received are four thicknesses of tendon intended for as many different classes of wounds.

EUCALYPTUS KINOS.[1]

Two samples of Eucalyptus kino from Australia were accompanied by the following note from the sender:

"*Eucalyptus rostrata* or red gum is very common throughout Australia. It is usually found along river courses and in marshy ground, attaining a height of 60 feet. The wood is used for upright posts and piles, as it is especially hard and durable, and withstands the action of water. It is our chief wood for street paving. The ruby-colored exudation or 'red gum,' Gummi rubrum, exudes from the bark, and has been miscalled Eucalyptus kino on account of its astringency. As first gathered it is not quite soluble, and has a certain amount of dirt, as per sample sent. This can be supplied at 3 shillings per pound. After treatment to make it quite soluble, as per sample sent, it can be supplied at 4 shillings 6 pence per pound. The soluble is listed in London at 7 shillings per pound. It is highly astringent and is used in diarrhœa, dysentery and relaxed conditions of the throat. It is better than kino, as it adheres better to mucous surfaces. It occurs in grains or small masses of a ruby or garnet-red color and transparent, has a rough astringent taste, and if chewed tinges the saliva red and sticks to the teeth. It is used as a lozenge, and with water and spirit as an astringent injection. It is used in suppositories, and, as tincture, it makes a good gargle. The fresh bark contains 7·8 per cent. of the kino or gum.

"Correctly speaking, 'kino' is the juice obtained from incisions in the trunk of *Pterocarpus marsupium*, evaporated to dryness."

[1] These notes were furnished us by William B. Marshall, Curator of the Philadelphia Museum.—EDITOR.

PICTET'S PROCESS FOR THE PURIFICATION OF CHLOROFORM.

By means of a double-walled cylinder, Pictet was able, with the aid of nitric oxide, to produce a temperature of — 120° C. In this cylinder chloroform seemed to solidify at — 63° C. He then built a larger container to hold 100 kilogrammes of chloroform, using a mixture of carbon dioxide and sulphurous acid, thus producing a temperature of — 80° C., but the chloroform failed to crystallize. After some experiments, it was found that chloroform congealed at — 83° C. instead of — 63° C. In his first experiment, the thermometer showed — 63° C., but the mass must have been at least — 83° C. "The higher temperature was produced by waves from the outer circle passing through the liquid and striking the thermometer, thus producing the higher temperature."

It had been found that commercial chloroform contained as much as 30 per cent. of impurity, and consisted of some of the chlorides of carbon, but chiefly of a combination, $CHCl_3$, possibly an isomer of chloroform. On exposing the 30 per cent. impurity to the rays of the sun, decomposition resulted in a few minutes. Recrystallized chloroform remained absolutely unchanged after several days' exposure to the sun.—1899, *Jour. Soc. Chem. Ind.*, *18*, 231.

L. F. KEBLER.

STERCULIA TOMENTOSA AND ITS GUM.

Under the name *M'beppe*, *Kongosita*, *Komikosita*, *M'boborg* and *Ici-ia-chixé*, the above-mentioned plant is well known in Central Africa, and its general characters—historical, botanical and commercial—are the subject of a recent elaborate essay by E. Heckel (*Repertoire de Pharm.*, 1899, 1). It is a tree about 10 metres high, with a gray and scarred bark, villous cordate-orbiculate to trilobate leaves, reddish pentamerous flowers and small (about 0·3 gramme each) seeds, which only contain oil and starch and are not used as are those from its congener *S. acuminata*. The sole native value of the plant arises from the gum exuded by the trunk, the yield of which is enhanced by artificial incisions. The gum resembles tragacanth, differing from it, however, in absence of starch and by forming with water a viscid liquid, rather than a jelly. Chemical examination shows it to consist largely of arabin. The gum is of interest from the standpoint of physiological botany, in that the yield is best from young and hardy plants.

H. V. ARNY.

EDITORIAL.

ENZYMIC AND SYMBIOTIC FERMENTATION.

While there have been a number of theories to explain fermentative changes, viz.: (1) The Acid Theory (of Pliny); (2) Contact Theory (Berzelius); (3) Mechanical or Physical Theory (Stahl); (4) Chemical Theory (Tromsdorff); (5) Galvanic Theory (Schweiger), and (6) Vital, Germ or Physiological Theory (Pasteur); it may be said that there have been but two views which have been to any great extent seriously considered in recent years, viz., the mechanical theory of which Liebig was the champion, and the vital theory of Pasteur, who discovered that fermentation is the result of the action of life without air ("*La fermentation est la conséquence de la vie sans air*"). It is a matter of common knowledge that the theory of Liebig was proven, by the results of the experiments of Pasteur, to be an error; and it may be said that these results at the same time illuminated the subject of the generation of life for the biological world and, furthermore, laid the foundation stones of the science of bacteriology.

Within the past few years the labors of E. Büchner have given rise to a new theory, known as the *enzyme theory* of fermentation. He has isolated an enzyme or ferment (zymase) from yeast with which alcoholic fermentation apparently can be produced. H. Abeles, however, took the position, a little more than a year ago, that the expressed juice from yeast plants with which Büchner worked really contained living fragments of the protoplasm of the yeast cell, and endeavored to explain the fermentative changes as due to this living plasma. In reply to Abeles, Büchner has shown rather conclusively in a number of experiments that the *plasma hypothesis* of the former is without foundation. More recently, A. Wroblewski, of Cracow, has made some studies on yeast juice by means of fractional coagulation, and he assumes that the enzyme is in that portion of the yeast which coagulates at 41°. J. Reynolds Green also confirms the researches of Büchner, and has shown that there is a ferment in the yeast cell which can be extracted and which will induce the alcoholic fermentation of sugar. These results of Büchner and others are extremely interesting, in that they disprove the two most important and commonly accepted points in the Theorie der Gährung (1879) of Nägeli. He distinguished the higher plants that produce distinctive ferment principles from the lower in which no such distinct principles had been discovered, and said of the latter "(1) that they had not yielded to any extracting medium anything that could effect fermentation in the absence of cells, and (2) that the products of their action are, 'without exception, less nutritious compounds,' and that they destroy the most nutritious substances. It was commonly accepted that, inasmuch as all of the important functions of the individual representing the unicellular plant were performed by the protoplasm of a single cell, the division of labor that can take place in a more differentiated structure is here impossible."[1] Krütsenberg, in some experiments (Vergleichend-physiologische Vorträge, Heidelberg), has apparently shown that "in the simplest forms the process of digestion is an intracellular one, not dependent on enzymes, but inherent in the protoplasm itself." While we cannot, in some instances at the present, deny the fermentative power of protoplasm, it has been shown by Büchner that in the so-called organized ferments unorganized fermentative principles are also present

[1] Greene, in *Annals of Botany*, 1893, p. 133.

which can be isolated, so that the zymase of yeast and the diastase of *Asperigillus oryzæ* correspond to the diastase of barley or the emulsin in almond.

At the same time that the enzyme theory of fermentation is being developed an equally interesting phase of the fermentation question from the biological point of view is coming to light in what is known as symbiotic fermentation. It was Schwendener who, in 1869, first conclusively showed the peculiar relationship existing between the algæ and fungi in what constitute the group of plants known as Lichens. When certain algæ and certain fungi were brought together under proper conditions, this relationship was shown to be not one of parasitism, but one of mutual benefit, and termed symbiosis. Since that time a symbiotic relationship in a large number of plants, as well as animals, has been observed. A good case of symbiosis is observed in the nodules on the roots of leguminous plants which are filled with bacteria. These latter penetrate the root hairs and perform in the living cells of the higher plant functions, which are of decided benefit. In the green infusoria, hydra, sponges, etc., is observed a symbiotic relationship between the alga and animal.

The investigators of recent years have shown that in the alcoholic fermentation of starch at least two organisms are at work, each doing its share towards producing the final products. "Van Laer has called attention to the symbiotic co-existence of two yeasts in many beers, explaining certain peculiar after-fermentations as due to the action of yeast on the medium improved for it by the other. The Japanese have long been in the habit of brewing a peculiar fermented liquor known as rice-wine or saké. Rice grains are steamed, and when cool infected with a mould fungus now known as *Asperigillus oryzæ*. When the rice is quite mouldy, at which time it emits a peculiar odor like pineapples, the starch is found to be turning rapidly into sugar, under the action of a diastatic enzyme secreted by the fungus. This decomposing rice is then placed in water and exposed to the action of a yeast, which rapidly ferments the sugar, and the alcoholic saké results. So closely is the yeast associated with the Asperigillus that, in practice, the alcoholic fermentation commences soon after the enzyme of the Asperigillus begins to hydrolyze the starch of the rice, and for some time a controversy existed as to whether the yeast was not really a part of the life history of the Asperigillus. Several observers have now shown, however, that we have here a striking case of symbiosis."[1] Similar cases of symbiosis are observed in the ginger-beer plant, only yeast and bacteria are here associated together, forming the clumps in the fermenting solutions.

A very complex system of symbiosis has been shown by the experiments of Omeliansky to be concerned in the circulation of nitrogen in nature. This author found that "if *Nitrosomonas*—the bacteria which oxidizes ammonia to nitric acid and *Nitrobacter*, the bacterium which further oxidizes nitrous to nitric acid—be sown together or separately on a medium containing organic nitrogen, no growth or change takes place. But if a bacterium capable of decomposing the organic nitrogenous medium, *e. g.*, *Bacillus ramosus*, is added to the above-mentioned *Nitrosomonas* and *Nitrobacter*, the associated three organisms are able to carry out all the processes and complete the cycle of

[1] Ottokar Shieweck (*Centr. Bakt. Par.*, I, ii, 782) supposes that the fermentation is caused by special yeasts, in part true yeasts (*Saccharomyces anomalus* and a yeast with round spores), which are mixed with Asperigillus. See also *Chem. News*, 1899, p. 174, and *Jour. Chem. Soc.* (abs.), 1898, p. 398.

nitrification; that is to say, *B. ramosus* breaks down the gelatine, and ammonia is formed; this is then oxidized to nitrous acid by *Nitrosomonas*, and the nitrous acid is further oxidized to nitric acid by *Nitrobacter*."

In endeavoring to ascertain some knowledge of the physiology of symbiosis, it is apparent that in the "closely associated symbiosis, such as those composing a lichen, the ginger-beer plant, or a clump of symbiotic bacteria or fungi, researches have made it practically certain that the provision of definite food materials by the one symbiant for the other may be an important factor, *e. g.*, an alga supplies a fungus with carbohydrates, or a fungus converts starch into the fermentable sugars which the associated yeast needs. In other cases the advantage derived is one of protection from some injurious agent, *e. g.*, the aërobic bacterium prevents the access of oxygen to the anaërobic one." Other factors besides these are at work causing symbiotic fermentation, and Marshall Ward discusses them in the *Chem. News*, 1899, p. 173. The consideration of the subject of both enzymic and symbiotic fermentation is of great importance in the arts and medicine, as it is these enzymes, as well as other products which are secreted by the fungi, bacteria and other organisms, which are either useful or harmful, and which may be produced in extent and kind depending upon the quantity or quality of food materials at command.

REVIEWS AND BIBLIOGRAPHICAL NOTICES.

MORPHOLOGY AND HISTOLOGY OF PLANTS. Designed Especially as a Guide to Plant Analysis and Classification, and as an Introduction to Pharmacognosy and Vegetable Physiology. Part I. The Morphology of Plants, by Henry H. Rusby, M.D. Part II. Plant Histology, by Smith Ely Jelliffe, M.D., Ph.D. With 693 Illustrations. Published by the authors.

It is probably the experience of all schools and colleges of pharmacy that the per cent. of matriculants holding high-school diplomas has been a constantly increasing one from year to year. Furthermore, it is gratifying to note that most high schools are giving more attention to the study of the sciences, especially botany, than heretofore, so much so, in fact, that some universities leave the teaching of the elements of systematic and physiological botany to them, and require botany for entrance. As this is the exception, however, rather than the rule, and as many students, especially in pharmacy, have not enjoyed more than a common-school education, it becomes absolutely necessary in all teaching institutions of pharmacy to more or less thoroughly rehearse those departments of botany deemed essential to the proper study of pharmacognosy and materia medica. A suitable text-book for the use of pharmacy students, one which is not burdened with useless, dry details, and at the same time is written in plain, easily understood language, has been really wanting in America. In the writer's opinion there is no text-book which so nearly supplies this want as the second edition of the above-named book. It may be truly said that this edition has been made wider in its scope by the addition of a large amount of matter of a more general character, but this is no objection, since it serves a larger class of students.

Quoting from the author's preface, "the additional matter consists in part of a more complete treatment of the original topics, but more especially in the

addition of chapters on methods of floral dissection and analysis, the description of flowers by means of diagrams and formulæ, the morphology and classification of cryptogamous plants, classification and nomenclature, and on the collection and preservation of specimens. In the chapters devoted to reproduction, special pains have been taken to make clear the homologies and affinities between the flowering and flowerless plants."

Especially well have the chapters on Botanical Classification and Analysis and Botanical Nomenclature been written. Some may argue against the detailed treatment of the chapter on Cryptogams, but, as stated by the author, this has been supplied to meet the wants of other than pharmacy students.

Part I is characterized by originality of treatment of the subject, clearness, accuracy, and conciseness of expression, and superb selection of illustrative material, much of which is familiar to the student of pharmacy. In fact, this portion of the work possesses an individuality that is decidedly pleasing.

Part II treats of the Microscope, the Plant Cell, Cell Contents, Cell Wall, and Tissue Systems. The opportunity for original treatment is apparently not so great as in Part I, since the subjects are treated in an order and manner very similar to that of several well-known German text-books. It is unfortunate that it was found necessary to resort to such wholesale borrowing of foreign cuts for use in an otherwise distinctly American text-book. Such cuts suffer more or less by reproduction, as a glance through the second part will demonstrate. At least in the copy at hand many of the finer details have been entirely obliterated. A redeeming feature, however, is the faithful observance of the principle "credit to whom credit is due," a principle which is not religiously observed by all writers. The text is clearly written and admirably serves the purpose for which it was intended. Taken as a whole, this book is a great improvement over the first edition, and constitutes a very valuable and timely contribution to botanical literature. It certainly deserves and will doubtless receive the same hearty reception as its predecessor.

J. O. SCHLOTTERBECK.

UNIVERSITY OF MICHIGAN.

MICROSCOPY AND MICRO-TECHNIQUE. By Albert Schneider, M.D., Ph.D., Professor of Botany, Pharmacography and Materia Medica, Northwestern University School of Pharmacy. Ninety-five illustrations. Large Octavo; 190 pages. Chicago: Chicago Medical Book Company. 1899.

A practical guide to the use of the microscope may be regarded as an essential to every student of natural science, theoretical or applied, whether engaged in a course of home-study, and without instructor, or under the best possible conditions. Quite a number of such books have appeared during the past decade, and this, the last of them, certainly deserves to rank among the very best. Perhaps the most characteristic feature of Professor Schneider's work is the manner in which it supplements a thorough analysis of the laws of optics by a series of simple and non-technical explanations. Most of such works have been faulty in one or the other of these directions. While some have depended so completely upon mathematical equations as to be fitted only for such students as have enjoyed a thorough and liberal preliminary education, others have been so superficial as to fail utterly to appeal to the latter class. None can complain of Dr. Schneider's mathematics, as to either quality or quantity, yet any student will find it easy to omit these explanations, yet without failing to get a

fair working idea of the essentials of practice. The development of the microscope is treated historically, and is supplemented by a history of glass manufacture. This order appears to be one of the few features of the book open to criticism, as it does not conduce to clearness. The allotment of space to the different subjects treated is as follows: Reflection of Light has ten pages; Refraction, four; Intensity, two; Simple and Compound Microscopes, treated as machines, thirty-six; Micrometers, Camera Lucida, Micro-Photographic Apparatus and Test-objects, ten; Optical and Working Properties, twelve; Manipulation and Care, nine. Then follows Part II, in which forty-five pages are devoted to Micro-technique. A concluding chapter of twenty-five pages, which might well have been called Part III, is devoted to the Normal and Abnormal Eye. Here the author's medical training is put to good service, and the inexperienced microscopist is led to a knowledge of the results of defective vision upon the use of the microscope, and how to avoid them. Some very practical suggestions concerning the care of the eyes are added. All the information is thoroughly classified, and the instruction well systematized. The language is clear, and no reader, even if ignorant of the high abilities of the author as a histologist, could fail to realize that he writes on a familiar subject, and out of the fulness of personal experience. A complete index of five double-column pages completes the usefulness of this thoroughly commendable volume.

H. H. RUSBY.

INDICATORS AND TEST PAPERS—THEIR SOURCE, PREPARATION, APPLICATION AND TESTS FOR SENSITIVENESS. A résumé of the current facts regarding the action and application of the indicators and test papers which have been proposed from time to time and are in present use in chemical manipulations, with a tabular summary of the application of indicators. Designed for the use of chemists, pharmacists and students. By Alfred I. Cohn, Ph.G. First edition. First thousand. 1899. 12mo. ix–249 pages. Cloth, $2. New York: John Wiley & Sons.

The book is divided into four parts. Part I, the introduction, contains general considerations, correct choice of indicators, application of indicators, action of indicators in other than aqueous liquids and the theory of the action of indicators.

Part II contains, in alphabetical order, the synonyms, source, preparation, properties and application of the various indicators considered.

Part III deals entirely with test papers, their preparation and application.

Part IV contains tables and a tabular summary of the principal indicators.

The object of this book is to give an up-to-date résumé of the various substances that have been employed as indicators in one form or another. The number of indicators considered is certainly comprehensive, but the author fails in a number of instances to bring his volume up to date. For instance, much of what is said concerning the influence of alcohol on indicators, on page 12, is based on a paper the conclusions of which have been shown to be the result of working with impure alcohol. In other words, *pure alcohol does not* appreciably affect the color reactions of most of the important indicators.

R. Schmitt's process for the manufacture of synthetic salicylic acid is not referred to in connection with this article, yet this method has probably superseded all others for manufacturing salicylic acid.

A number of errors have also crept in. The melting point of phenolphthalein (page 127) is given as 150° C., whereas it should be 250° C. The melting point of alizarin is about 282° C., instead of 215° C. (page 23). The formula for sodium hydroxide (page 223) is written NAOH, and potassium ferricyanide (page 142) is written K_6FeCy_{12}. The value of the book would be much enhanced if references to the original literature were given.

The style is generally clear, the type neat and the paper of good quality.

Notwithstanding some omissions and errors, the book contains much useful information collected from various sources of literature, and should find a place in every chemical library.

L. F. KEBLER.

PROCEEDINGS OF THE TWENTY-FIRST ANNUAL MEETING OF THE MISSOURI PHARMACEUTICAL ASSOCIATION, held in Jefferson City, June 6–9, 1899.

The following are the titles of the papers read: "Chemical Pharmacist or Pharmacist's Chemicals," by J. F. Lewellyn; "Commercial Pharmacy," by O. F. Bausch; "Contributions, from Date of Organization," by Ambrose Mueller; "Does It Pay the Pharmacist to Make Compressed Tablets?" by Ambrose Mueller; "Does the Attorney-General Understand the Situation?" by Francis Hemm; "Financial Points for a Retail Druggist," by O. T. Claus; "How to Make the Drug Business Pay," by Wm. Mittelbach; "Glucose Investigation," by C. M. T. Klie; "How to Secure the Family Trade for Spices and Flavoring Extracts," by G. H. J. Andreas and Wm. Mittelbach, independently; "Report on Metric System," by H. M. Whelpley; "Suggestions to Pharmacopœial Committee," by Francis Hemm; "Revision of the Pharmacopœia and the Retail Druggist," by G. D. Hinrichs; "Prescription Scale and Quantitative Chemical Work of the Druggist," by C. G. Hinrichs; "Women in Pharmacy," by F. de Wyl.

MINUTES OF THE PHARMACEUTICAL MEETING.

The regular monthly pharmaceutical meeting was held Tuesday, December 19th, in the Museum of the College, with James T. Shinn, Ph.M., in the chair.

Dr. A. R. L. Dohme, of Baltimore, was the first speaker on the programme and read a highly instructive paper on "The History of the Constitution of the Alkaloids." (See page 9.)

In introducing Dr. Dohme to the audience the chairman alluded to the educational advantages which he enjoyed and also to his special interest in the study of the alkaloids, both of which qualifications enabled him to speak with authority on the subject chosen.

In some preliminary remarks on the nature of his paper, Dr. Dohme said it would be found to deal largely with theory, but that this was a feature due to the necessity of having theories concerning the alkaloids before working out their constitution.

The paper elicited considerable discussion, and among those taking part in it were the chairman, Professors Moerk and Kraemer and Messrs. Kebler, Haussmann and Boring. Professor Moerk thought the address an excellent one and very opportune in one respect, as the students of the third year class, many of whom were present, are now being instructed in organic chemistry and just

about taking up the subject of the alkaloids. He, furthermore, moved that a vote of thanks be tendered Dr. Dohme and this motion was unanimously adopted.

Professor Kraemer was particularly glad that in the conclusion to his paper the author made a practical application of the knowledge involved in working out the theories concerning the alkaloids, for too often knowledge of this character is not appreciated at its full value by those interested in practical and commercial questions.

Referring to the comparison which Dr. Dohme made of the formulas of hydrastine, narcotine and papaverine, Mr. Kebler said that it is well known that the introduction of a single OH group will change the nature of some organic compounds very materially.

Dr. Dohme replied that in some of the simpler compounds an OH group might cause a considerable difference, but when complex substances like the alkaloids are considered, and an endeavor is made to trace some connection or some relation between structure and organic effect, the difference caused by such a group becomes less marked.

In answer to a query by Mr. Haussmann as to the cause of the black color produced when pilocarpine and cocaine are mixed with calomel, Dr. Dohme said that pilocarpine is an ammonia derivative and hence affects calomel, and in case of cocaine he thought that perhaps the CHO group would cause it to have a reducing action on calomel.

Charles H. La Wall was next on the programme and read an interesting paper entitled "The Herb and Drug Vendors on the Sidewalks of Philadelphia," which will be published in full in the February issue of this JOURNAL. Mr. La Wall said that he had been collecting data on this subject for several years and that he had become very much interested in it. Somewhat surprising was the statement made by him that 75 per cent. of the official drugs are growing within a radius of a few miles of Philadelphia, and also that more than 50 per cent. of the official drugs are sold on the streets of the city by persons who earn a livelihood by collecting them and preparing them for sale. The paper was accompanied by specimens and photographs of some of the vendors and their wares.

Professor Kraemer said that personally he was very much pleased that Mr. La Wall had taken up this subject. He said that he had known of persons going regularly to some one of these vendors for certain products on account of their excellent quality. In this connection he remarked upon the different channels into which the pharmacist's work is going and urged upon those present the necessity of obtaining a knowledge of just such subjects as were indicated in this paper. A vote of thanks was likewise tendered Mr. LaWall.

Mr. C. Carroll Meyer spoke of the cheapness and neatness of the packages of crude drugs put up by wholesale houses for retail purposes, but said that their quality was not likely to be known to the pharmacist.

Mr. E. M. Boring exhibited a sample of oil of orange, which, though quite old, was still in a state of preservation. This he said was due to the addition first of a small quantity of alcohol and then of water. Mr. Shinn said that he had also used a similar method—the difference being that he washed out the alcohol from the oil with the water, after which the oil kept very well.

On motion, the meeting adjourned.

FLORENCE YAPLE,
Secretary pro tem.

✻ CLASSES ✻

OF THE

PHILADELPHIA COLLEGE OF PHARMACY,

Seventy-ninth Annual Session, 1899-1900.

FIRST YEAR CLASS LIST.

Name.	*Place.*	*State.*	*Preceptor.*
Ackerman, Wm. Brown,	E. Mauch Chunk,	Pa.	Geo. L. Carnan.
Allen, Edwin Cullom,	Philadelphia,	Pa.	Wm. Egolf.
Alston, Wm. Algernon,	Haygood,	S. C.	
Anderson, Leon Cornelius,	Reading,	Pa.	H. H. Kline.
Ashmead, Virden Peter,	Philadelphia,	Pa.	Anna F. Ashmead.
Bacon, Vela,	Freehold,	N. J.	Bacon & Pittinger.
Baer, Herbert Oscar,	Wheeling,	W. Va.	W. S. Dixon.
Bair, Edward Elmer,	York,	Pa.	J. J. Weakley.
Baker, Daniel,	Belle Vernon,	Pa.	
Banta, Clarence La Rue,	Hanover,	Ind.	Dr. H. B. Morse.
Baum, Edward Eugene,	Batavia,	Ohio.	
Bell, Herman Alonzo,	Philadelphia,	Pa.	
Beegle, David Elmer,	Bedford,	Pa.	H. C. Blair.
Berberich, Joseph Herman,	Stein,	Germany.	J. Moffet, Jr.
Bibby, David Boone,	Catawissa,	Pa.	
Binder, Arthur Henry,	Meadville,	Pa.	T. W. Reuting.
Blew, Robt. St. Clair,	Bridgeton,	N. J.	C. W. Shull.
Blough, Elijah Roberts,	Johnstown,	Pa.	A. L. Yoder, M.D.
Bornemann, John Alexander,	Westphalia,	Germany.	H. M. Campbell.
Bowers, Robt. Ellerslie,	Mechanicsburg,	Pa.	E. C. Stout.
Boyer, Walter Ernest,	Danville,	Pa.	F. Ross Harmer.
Brightbill, Jonathan Furl,	Bedford,	Pa.	Irvine & Co.
Brock, George William,	Lockwood,	Mo.	
Brown, Herbert Wills,	Woodbury,	N. J.	J. W. Merritt.
Brown, Horsey Pierce,	Wilmington,	Del.	Z. James Belt.
Brown, Joel Daniel,	Philadelphia,	Pa.	W. A. Rumsey.
Brunhouse, Harry Franklin,	York,	Pa.	F. Brunhouse.
Bryant, Jas. Robeson,	E. Stroudsburg,	Pa.	W. H. Umstead.
Buckley, Martha,	Norristown,	Pa.	W. A. Costen.
Caden, Alice Beatrice,	Lexington,	Ky.	Adams & Morford.
Carmany, Jay Le Van,	Harrisburg,	Pa.	F. H. Boer.
Carter, Fredk. Phillips,	Beverly,	N. J.	A. W. Taylor.
Catlin, Joseph Albert,	Churchill,	Md.	J. J. Kelley.
Clemmer, John Krupp,	Lansdale,	Pa.	Jas. Williamson.
Collins, John Joseph,	Williston,	Me.	Wakefield Brothers.
Comfort, Carlton Chapell,	Philadelphia,	Pa.	Dr. J. W. Harrigan.
Craven, Alfred Young,	Bridgeport,	Pa.	H. L. Randall.
Crawford, Thos. Foster,	Camden,	N. J.	C. B. McLoughlin.
Croft, Clarence,	Chambersburg,	Pa.	G. L. Giger & Co.
Crothers, Anthony Brooks,	Cecil Co.,	Md.	J. L. Crothers
Dana, Lawrence Wellington,	Kane,	Pa.	E. H. Watkins.
Davis, Joseph Randall	Philadelphia,	Pa.	Dr. W. S. McGhee

Name.	*Place.*	*State.*	*Preceptor.*
Dickinson, Ralph Brinton,	Parkersburg,	Pa.	J. B. Thompson.
Dewees, Everett Wheeler,	Philadelphia,	Pa.	E. C. Stout.
Dix, Robt. J. Gillingham,	Moorestown,	N. J.	G. H. Wilkinson.
Donoghue, Theressa Veronica,	Girardville,	Pa.	Dr. Jas. Donoghue.
Dougherty, Eugene R.,	Reading,	Pa.	Chas. Rentschler, Jr.
Doughty, Robert M.,	Millville,	N. J.	
Douglass, John Xavier,	Philadelphia,	Pa.	D. J. Reese.
Downs, Wm. Joseph,	Coaldale,	Pa.	John H. Bailey.
Dufford, John Albert,	West Sunbury,	Pa.	L. S. A. Stedem.
Eckels, Nathaniel Ort,	Shippensburg,	Pa.	A. L. Metz.
Evans, Thomas John,	Plymouth,	Pa.	G. J. Durbin.
Eves, Chas. Scott,	Millville,	N. J.	C. S. Ely.
Evrard, John Joseph,	S. Bethlehem,	Pa.	Kennedy & Burke.
Faust, Peter Winner,	Claussville,	Pa.	H. L. Keiper.
Feeney, Patrick Joseph,	Germantown,	Pa.	A. B. Newton.
Fetterolf, C. Fredk. Garfield,	Ashland,	Pa.	H. L. Stiles.
Filman, Walter Theodore,	Warwick,	Pa.	H. L. Klopp.
Fitch, Jas. Clarence,	Philadelphia,	Pa.	Dr. P. Fitch.
Fleischer, Wm. Paul,	Philadelphia,	Pa.	F. E. Johnson, M.D.
Foehl, Philip C.,	Lancaster,	Pa.	H. H. Ross.
Fox, Irvin Berry,	Lebanon,	Pa.	J. L. Lemberger & Co.
Fox, Joseph P.,	Philadelphia,	Pa.	P. P. Fox, Sr.
Fried, Percy,	Allentown,	Pa.	F. P. Semmel, Jr.
Fuller, Royston Chas. Tupper,	Amherst,	N. S.	R. C. Fuller & Co.
Gagan, George,	Wilmington,	Del.	H. C. Blair.
Gage, Luther Hendrick,	Leraysville,	Pa.	W. D. Johnson.
Garman, Ovy William,	Nora Springs,	Ia.	J. H. Atkinson & Co.
Gearhart, Malcolm Zieber,	Reading,	Pa.	S. S. Stevens.
Gehringer, Edwin Franklin,	Allentown,	Pa.	O. J. J. Haines.
Geron, Yeatman,	Huntsville,	Ala.	J. D. Humphrey & Son.
Gettel, John Ralph Elkrode,	Shippensburg,	Pa.	J. C. Altick & Co.
Giles, Edward Wm.,	Columbia,	S. C.	J. J. Leggett.
Goodman, Edith Morton,	Denver,	Col.	Dr. Susan Hayhurst.
Goring, Wyatt Edward,	Wappinger Falls,	N. Y.	Geo. Howarth.
Greenberg, Dora,	Roumania,	Europe.	
Hamilton, Harry Schroyer,	Mechanicsburg,	Pa.	Dr. Long.
Hand, Reu,	Cape May,	N. J.	Dr. Mecray.
Harrington, Bertram John,	New Brunswick,	Canada.	J. C. Perry.
Handwork, Francis Collins,	Birdsboro,	Pa.	R. Clark.
Hartung, Edward Wm.,	Philadelphia,	Pa.	H. S. Butz.
Hawkins, Louis Jefferis,	Coatesville,	Pa.	W. S. Young.
Hayes, John Gilbert,	St. Clair,	Pa.	Harry Davis.
Heffelfinger, Wm. Edward,	Reading,	Pa.	J. H. Stein.
Henderson, Luther Bateman,	Newport,	N. J.	
Hendrickson, Raymond,	San Francisco,	Cal.	W. H. Gano.
Hertzler, Norman Eberly,	Philadelphia,	Pa.	Fred. Brown Co.
Hertzler, Oliver Henry,	Lancaster,	Pa.	C. A. Heinitsh, dec'd.
Hibbs, Wm. Buckman,	Newtown,	Pa.	Wm. R. Elliott.
Hilliard, Bayard,	Vincentown,	N. J.	F. S. Hilliard.
Hougendobler, Harry Smaltz,	Columbia,	Pa.	W. H. Hickman.
Irvin, John Henry,	Philadelphia,	Pa.	A. Wilson.
Jaego, Harry W. Garfield,	Millville,	N. J.	P. F. Haas.
Jefferis, Charles Albert,	Philadelphia,	Pa.	Funk & Groff.
Jones, Howard Harlan,	Norristown,	Pa.	Atwood Yeakle, Ph.G.
Kane, Augustin Francis,	Brooklyn,	N. Y.	Dr. F. F. Druding.
Kellar, William Albert,	Cripple Creek,	Col.	Central Drug Co.
Kennedy, Wm. Morton,	Philadelphia,	Pa.	C. J. Siglinger.
King, Charles Tomlinson,	Wellsborough,	Pa.	J. N. G. Long.
Kirk, Frank Hall,	Curwensville,	Pa.	Shinn & Baer.
Klinka, Adolph Jules,	Philadelphia,	Pa.	

Name.	Place.	State.	Preceptor.
Knabb, Milton H.,	Reading,	Pa.	W. H. Raser.
Knauss, Howard James,	Allentown,	Pa.	Dr. R. C. Peter, Ph.G.
Koller, Charles Joseph,	Altoona,	Pa.	C. G. Neely.
Kyle, Janet.	Milroy,	Pa.	
Kyle, Christian Bauer,	Middletown,	Pa.	C. E. Bowers.
Lebegern, Barton,	Columbia,	Pa.	Eberly Brothers.
Lescure, Anna R.,	Philadelphia,	Pa.	
Lewis, Herbert Willard,	Springfield,	Mass.	Harry P. Elvey.
Lide, Leighton Elba,	Columbus,	Miss.	Mayo & Weaver.
McGarrah, Wm. Henry, Jr.,	Scranton,	Pa.	T. D. McPhee.
McGregor, Albert Dell,	Maywood,	Ill.	G. M. Beringer.
Marcus, Simon,	Philadelphia,	Pa.	W. A. Shannon.
Margolin, Fannie Bezman,	Philadelphia,	Pa.	J. H. Hackett.
Martin, Charles Edward,	Columbia,	Pa.	E. C. Shafer.
Martin, Frederick Adams,	Atlantic City,	N. J.	J. V. Townsend.
Martin, John M.,	Birmingham,	Ala.	W. R. Gunn.
Matlack, Walter Ball,	Bridgeton,	N. J.	G. Y. Wood.
Meals, Ira Dale,	Harrisburg,	Pa.	Dr. C. T. George.
Meredath, Wilbur Curtis,	Wagontown,	Pa.	R. H. Lackey.
Metzler, Oscar Leroy,	Harrisonville,	Pa.	J. A. Ferguson.
Mewhorter, Harry Stuart,	Norristown,	Pa.	W. A. Costen.
Miller, Roy L.,	Union Bridge,	Md.	
Morgan, Wm. Ellis,	Eldorado,	Ark.	Dr. W. H. Goodwin.
Munger, Lewis,	Chester,	Pa.	D. P. Madden.
Murphy, Dennis Arthur,	Monson,	Mass.	G. L. Keeney.
Myers, Luther Melanothon,	Carlisle,	Pa.	B. F. Emrick.
Noble, Harry Carty,	Manayunk,	Pa.	H. M. Leveriug.
Oberly, John Shimer,	Easton,	Pa.	A. L. Serfass.
O'Hanlon, Joseph Thornley,	Pennington,	N. J.	G. W. Scarborough.
Orr, James Alexander,	Belfast,	Ireland.	S. H. Shingle.
Parker, James Heber,	Reading,	Pa.	J. H. Stein.
Phillips, Eliot Earle,	Philadelphia,	Pa.	W. P. Bender.
Quin, Vincent De Paul,	Lansford,	Pa.	J. A. Quin.
Ramsaur, David Wilfong,	Palatka,	Fla.	M. W. Stewart.
Raum, Harry Angle,	Shippensburg,	Pa.	D. H. Ross.
Reeve, Albert Warfield,	Elmer,	N. J.	J. M. Garrison, Jr.
Reice, Isaac Stephen,	Bloomsburg,	Pa.	Moyer Brothers.
Renaker, Houston,	Cynthiana,	Ky.	J. M. Renaker.
Rhoder, Geo. Washington,	Newark,	Del.	Dr. J. B. Butler.
Rigg, Bernard,	Keansburg,	Ill.	
Robinson, David Crogman,	Philadelphia,	Pa.	H. M. Minton.
Robinson, Thomas Holmes,	Bealston,	Va.	F. J. Lammer.
Roeder, Morris Albert,	Schuylkill Haven,	Pa.	C. S. Commings.
Roessler, Harry Link,	Philadelphia,	Pa.	H. A. Smith.
Roessler, Henry Wayman,	Philadelphia,	Pa.	W. H. Laubach, Jr.
Rudolph, Harold Clarence,	Pottsville,	Pa.	J. P. Frey.
Schiesser, Harry William,	Philadelphia,	Pa.	Dr. P. M. Kelly.
Scott, Walter Edward,	Pomeroy,	Pa.	J. G. Long.
Seal, John Horace,	Swarthmore,	Pa.	Dr. A. K. Morton.
Seeley, Chester Belting,	Bridgeton,	N. J.	G. H. Whipple & Son.
Sharp, Wm. Luther,	Keensburg,	Ill.	J. T. Legier.
Shaw, Saml. Frederick,	Philadelphia,	Pa.	G. B. Evans.
Shaw, Wm.,	St. Louis,	Mo.	
Slobig, Charles Henry,	Ashland,	Pa.	R. J. Williams.
Smith, Henry Wm.,	Pottstown,	Pa.	E. S. Beshore.
Smith, Karl Waller,	Marietta,	Pa.	R. W. Cuthbert.
Smith, Wm. David Harris,	Jonesboro,	Tenn.	J. B. Park.
Soken, Joseph Lewis,	Zitsmir,	Russia.	Dr. Seldes.
Stauffer, John Keeler,	Goodville,	Pa.	C. G. Treichler.
Stolz, David,	Syracuse,	N. Y.	G. I. Thorpe.

Name.	*Place.*	*State.*	*Preceptor.*
Strauss, Robert Franklin,	Womelsdorf,	Pa.	F. I. Landis.
Stuver, Henry Wm.,	Fort Collins,	Col.	W. W. Scott.
Swartz, Wm. Luther,	Carlisle,	Pa.	G. W. Sipe.
Swineford, Ernest Clarence,	Mifflinsburg,	Pa.	Dr. F. B. Brubaker.
Taylor, James Alfred,	Flat Rock,	S. C.	J. A. Taylor.
Terne, Bruno Henry, Jr.,	Chicago,	Ill.	H. B. Terne.
Thomas, George Carroll,	Lima,	Pa.	Dr. Wingender.
Toulson, John M.,	Chestertown,	Md.	M. A. Toulson.
Trost, Wm. Christian,	Ashland,	Pa.	A. Schoenenberger.
Tyler, Ephraim Shaw,	Bridgeton,	N. J.	W. A. Rumsey.
Ulrich, Ralph Thomas,	Manheim,	Pa.	E. E. Gibble, M.D.
Waldenberger, William,	Manayunk,	Pa.	Louis Waldenberger.
Walther, Philip,	Meadville,	Pa.	V. W. Eiler.
Warner, Harold Clevenger,	Pemberton,	N. J.	Davis & Bro.
Weidemann, George Buzby,	Philadelphia,	Pa.	C. A. Weidemann.
Weigester, Wilson,	Troy,	Pa.	Carpenter & Pierce.
Welch, William Herbert,	Philadelphia,	Pa.	M. J. Wilson.
West, Emile,	Chambersburg,	Pa.	Jno. S. Zapirtz.
White, Albert Russell,	Caribou,	Me.	F. L. White.
Wildasin, Guy Otto,	Dayton,	Ohio.	A. L. Green.
Williams, Morrison Patton,	Charlotte,	N. C.	Shinn & Baer.
Wilson, Oscar Herman,	Frankford,	Phila.	H. J. Siegfried.
Winkler, Max Erwin,	Philadelphia,	Pa.	Max Winkler.
Winstanley, John,	Philadelphia,	Pa.	B. A. Wissler.
Wisegarver, Oscar Kline,	Quarryville,	Pa.	T. M. Sohrer.
Wollaston, Byron Parker,	Kennett Square,	Pa.	Wm. C. Pierce.
Woodill, Robt. Franklin,	Boston,	Mass.	C. E. Keeler.
Worthington, J. W. Wolfe,	Philadelphia,	Pa.	Chas. H. Clark.
Ziegler, Chas. Norman,	Gettysburg,	Pa.	L. Genois.
Ziegler, Wm. Lodge, Jr.,	Steelton,	Pa.	W. L. Ziegler, M.D.
Zinn, Edwin Clarence,	Carlisle,	Pa.	W. F. Horn.

SECOND YEAR CLASS LIST.

Name.	*Place.*	*State.*	*Preceptor.*
Alden, Harley Roscoe,	Auburn,	Me.	Dr. A. J. Pollard,
Barnett, Eldredge Ewing,	Cape May City,	N. J.	D. C. Guthrie.
Bell, Robert Nevins,	Kearney,	Neb.	S. A. D. Henline.
Benner, Fredk. James,	Bethlehem,	Pa.	P. Kempsmith.
Boesch, Theodore Karl,	York,	Pa.	A. H. Lafean & Bro.
Boltz, Paul Kline,	Lebanon,	Pa.	E. K. Boltz.
Boysen, Theophilus H., Jr.,	Egg Harbor,	N. J.	T. H. Boysen, M.D.
Brenner, Frederic A.,	Kylertown,	Pa.	L. C. Funk.
Cather, Frank L.,	Chester,	Pa.	Wm. H. Farley.
Collins, Lane Verlinden,	Philadelphia,	Pa.	Jno. P. Frey.
Cone, Earl Hobart,	Batavia	N. Y.	N. S. & J. J. Patterson.
Converse, Howard Romaine,	Picture Rocks,	Pa.	Moyer Brothers.
Corson, Harry Le Roy,	Jersey Shore,	Pa.	B. E. Staples.
Davis, William Brown,	Edwardsdale,	Pa.	D. E. Lewis.
Dean, Chester Clayton,	Philadelphia,	Pa.	C. R. Haig.
Dodson, Henry Malcolm,	Delta,	Pa.	M. L. Holloway.
Dunn, Edwin Alfred,	Meadville,	Pa.	P. H. Utech.
Dutton, John Fredrick,	Philadelphia,	Pa.	H. Minton.
Eckels, Paul,	Decatur,	Ill.	Chas. A. Eckels.
Eddy, Roswell Martin,	Philadelphia,	Pa.	
Eppler, George Theodore,	Philadelphia,	Pa.	E. E. Wilson & Co.
Fegley, Florence Augusta,	Allentown,	Pa.	O. Fegley & Bro.
Fegley, John Stauffer,	Allentown,	Pa.	O. Fegley & Bro.

Name.	*Place.*	*State.*	*Preceptor.*
Fischer, Adolph Gustav,	Philadelphia,	Pa.	Albert Oetinger.
Fisher, George Calvin,	Philadelphia,	Pa.	Edwd. Fisher.
Fleming, Samuel Clarkson,	York,	Pa.	Jas. C. Perry.
French, Rolland Hall,	Salem,	Ohio.	Bolger & French.
Garber, E. Franklin Weaver,	Mt. Joy,	Pa.	H. G. Haring.
Gliem, Harry Charles,	Hazleton,	Pa.	McNair & Hoagland.
Goodyear, Harry J.,	Cornwall,	Pa.	J. L. Lemberger.
Graham, Willard Rice,	Philadelphia,	Pa.	Smith, Kline, French Co.
Grove, Harry Ross,	Alexandria,	Pa.	R. T. Blackwood.
Harbord, Kittie Walker,	Salem,	Ore.	D. J. Fry.
Harris, Wm. K. Garfield,	Altoona,	Pa.	Dr. F. Barr.
Hassinger, Samuel Reed,	Philadelphia,	Pa.	S. E. R. Hassinger.
Haydock, Mabelle,	Philadelphia,	Pa.	Susanna G. Haydock.
Headings, Prestie Milroy,	Reedsville,	Pa.	Dr. H. W. Sweigart.
Highfield, Herbert Monroe,	Zanesville,	Ohio.	Bailey Drug Co.
Hinski, Oscar,			
Hoffert, Charles Edward,	Lancaster,	Pa.	C. E. Keeler.
Hoffman, Ira Calvin,	Johnstown,	Pa.	H. B. Heffley.
Houston, Franklin Paxson,	Philadelphia,	Pa.	R. T. Young.
Hubler, Guy Garfield,	Gordon,	Pa.	J. E. Gregory.
Hughes, Julia Pearl,	Charlotte,	N. C.	J. M. Porter.
Janisch, Fredk. Wm.,	Philadelphia,	Pa.	Emil Jungmann.
Jetton, James Stuart,	Dyer,	Tenn.	Hays & Grigsby.
Klopp, Edward Jonathan,	Richland,	Pa.	H. C. Blair.
Knerr, Charles George,	Allentown,	Pa.	J. W. Shoemaker & Co.
Kraus, Otto S.,	New Haven,	Conn.	Otto Kraus.
Leiby, Howard E.,	Philadelphia,	Pa.	F. G. Mumma.
Lesher, Benjamin Porter,	Chambersburg,	Pa.	And'w Blair & Co.
Levering, John Hartranft,	Norristown,	Pa.	J. C. Life.
Lewis, Fielding Otis,	Hibbardsville,	Ky.	R. M. McFarland.
Liebert, Lewis William,	Philadelphia,	Pa.	H. C. Clapham.
Luebert, Fred'k George,	Philadelphia,	Pa.	E. G. F. Mickley.
Luddy, Jas. Darrah,	Philadelphia,	Pa.	F. P. Streeper.
McClintock, Geo. Washington,	Key West,	Fla.	H. C. Blair.
McClurg, Benjamin Hoffer,	Elizabethtown,	Pa.	A. H. Bolton.
McDermott, Rob't Joseph,	Trenton,	N. J.	A. S. Wickham.
McFadden, Warren Lester,	Williamsport,	Pa.	Duble & Cornell.
McLaughlin, Harry Aloysius,	Philadelphia,	Pa.	N. Richardson.
McPhee, John James,	New Glasgow,	N. S.	T. D. McPhee.
Manger, Harry Fillmen,	Pottstown,	Pa.	J. D. Seiberling.
Metcalf, Hiram Kennedy,	Greencastle,	Pa.	C. H. Beetem.
Michels, Victor Clyde,	Albion,	Ill.	B. F. Michels.
Murphy, Edwin Mason,	Macon,	Miss.	T. S. Murphy.
Musser, Guy Musselman,	Witmer,	Pa.	R. W. Cuthbert.
Nauss, George Hill,	Steelton,	Pa.	W. K. Martz.
Penrose, Thos. William,	Philadelphia,	Pa.	F. W. E. Stedem.
Picking, Jr., Jacob Sylvester,	Somerset,	Pa.	F. C. Kreis, M.D.
Pittinger, Charles A.,	Freehold,	N. J.	E. G. Bacon.
Pfleiger, Adam W.,	York,	Pa.	A. L. Ziegler.
Pollins, Harry Geo. Lomison,	Greensburg,	Pa.	S. P. Brown.
Post, Arthur Edward,	Towanda,	Pa.	F. E. Post.
Raser, Jr., Wm. Heyl,	Reading,	Pa.	John B. Raser.
Redcay, Franklin,	Pottsville,	Pa.	Dr. E. D. Miller.
Reinhart, J. Quigley,	Shepherdstown,	W. Va.	H. B. Morse.
Reynolds, Clarence Hyatt,	Reynoldsville,	Pa.	S. Reynolds, M.D.
Rhoads, Luther K.,	Reading,	Pa.	C. H. Raudenbreah.
Rinker, William,	Hellertown,	Pa.	F. E. Jacobson.
Roberts, Geo. Wm.,	Philadelphia,	Pa.	W. R. Warner & Co.
Roberts, John A.,	Beverly,	N. J.	Dr. A. W. Taylor.
Rogers, Walter Clyde,	West Chester,	Pa.	F. P. Rogers.

Name.	*Place.*	*State.*	*Preceptor.*
Ryan, Thomas Andrew,	Susquehanna,	Pa.	W. S. Mitchell.
Saul, Irvin Ellswerth,	Windsor Castle,	Pa.	J. W. Pechin.
Schepp, Wm. Frederick,	Wheeling,	W. Va.	G. H. Ebeling.
Schmucker, A. Alexander,	Allentown,	Pa.	J. L. Crothers.
Schneider, Emil Sebastian,	Philadelphia,	Pa.	Philip Goll.
Schooley, Joseph Griggs,	Montgomery,	Pa.	J. L. Miller.
Scott, Wm. Henry,	Waynesburg,	Pa.	Dr. Brock.
Shafer, Clarence Eugene,	Altoona,	Pa.	H. L. Stiles.
Shannon, Byron Guest,	Pennsgrove,	N. J.	A. C. Schofield.
Shaver, D. Oscar,	Altoona,	Pa.	C. C. Meyer.
Sheffer, Wm. W.,	Dillsburg,	Pa.	Lawson C. Funk.
Shenkle, Albert Philip,	Phœnixville,	Pa.	M. R. Shenkle.
Shields, Percy Way,	West Chester,	Pa.	M. W. Bowman.
Skillman, Lionel Gilleland,	Philadelphia,	Pa.	Shoemaker & Busch.
Slocum, Chas. Evan,	Ouray,	Col.	E. E. Stratton.
Spears, Edwd. Gibson,	Reading,	Pa.	H. H. Kline.
Sprague, Hugh Boleyn,	Salt Lake City,	Utah.	Druel & Franken.
Steever, Wm. Forsaith,	Millersburg,	Pa.	Chas. C. Steever.
Stern, Wilson Clinton Ammon,	Philadelphia,	Pa.	D. B. Richards.
Stoudt, Irwin Sylvester,	Obold,	Pa.	Geo. F. Wood.
Strathie, Alex. John,	Handcross,	England.	Wm. J. Jenks.
Texter, Charles Henry,	Perkasie,	Pa.	Harry Neamand.
Thomas, Wallace Crouch,	Thomas,	Pa.	M. B. Fritz.
Thompson, Samuel,	Philadelphia,	Pa.	
Tingle, John Beard,	Dayton,	O.	Ed. M. Boring.
Townsend, Wm. Sidney,	Pocomoke,	Md.	H. N. Willis.
Tyler, Joseph Clark,	Mt. Sterling,	Ky.	R. C. Lloyd.
Urffer, Samuel,	South Bethlehem,	Pa.	H. W. Sheets.
Van Gelder, Levi,	Petersburg,	N. J.	C. B. McLaughlin.
Watson, Herbert James,	Wilmington,	Del.	H. K. Watson.
Wolfer, William Conrad,	Philadelphia,	Pa.	Ed. C. Stout.
Wolfinger, John Philip,	Reading,	Pa.	H. J. Schad.
Ziegler, C. Harry,	York,	Pa.	N. B. Fry.

THIRD YEAR CLASS LIST.

Name.	*Place.*	*State.*	*Preceptor.*
Albright, Allen Enos,	Allentown,	Pa.	W. L. Hatzell.
Anderson, George Charles,	Meadville,	Pa.	A. S. Ballinger.
Andrews, Wm. Hall,	Woodstown,	N. J.	G. M. Andrews.
Austin, Chas. Howard,	Woodstown,	N. J.	Theo. Campbell.
Baker, Maineard Lesher,	Cowan,	Pa.	C. W. Warrington.
Barker, Laura A.,	Houtzdale,	Pa.	B. W. Wood.
Bartholomew, Arthur,	Golden City,	Col.	J. M. Higgins.
Bayles, John Wyckoff,	Mt. Holly,	N. J.	
Beatty, Arthur William,	St. Louis,	Mo.	H. C. Blair.
Bishop, Wm. H. Pancoast,	Carversville,	Pa.	J. H. Bishop.
Blew, Jos. Oscar,	Bridgeton,	N. J.	C. F. Dare & Son.
Borrowes, Geo. Henry,	Philadelphia,	Pa.	D. Jamison.
Bosler, Harry Ellis,	Olean,	N. Y.	J. C. Welsh.
Bowers, Howard Levin,	Tuxton,	Pa.	J. C. Perry.
Branin, Manlif Lewis,	Millville,	N. J.	C. B. McLaughlin.
Brookes, Virginia Cade,	Waelder,	Tex.	S. Hayhurst.
Brooks, Walter.	Quarryville,	Pa.	T. M. Rohrer.
Buckman, Wm. Watson,	Newtown,	Pa.	H. Cox.
Burchfield, Wm. Clinton,	Pottsville,	Pa.	R. J. Williams.
Carey, Harris May,	Wyoming,	Del.	M. O. Harris.
Cartwright, Sanford Warren,	Fresno,	Cal.	J. L. Crothers.

Name.	*Place.*	*State.*	*Preceptor.*
Casperson, Henry Lyle,	Clayton,	Del.	W. R. Keys.
Connell, Frank Joseph,	Pottstown,	Pa.	
Cook, Ernest Fullerton,	Waynesboro,	Pa.	G. M. Beringer.
Corson, Thomas Clark,	Philadelphia,	Pa.	W. J. Scott.
Crawford, William Harvey,	Ashbourne,	Pa.	
Dentler, Roy W.,	Turbotville,	Pa.	F. W. Ely.
Desch, Edward Allen,	Fogelsville,	Pa.	C. J. Biddle.
Dietz, Harry Edgar,	Lock Haven,	Pa.	G. W. Mason.
Doake, Robert Stewart,	Philadelphia,	Pa.	Theodore Campbell.
Dooley, John Joseph,	Plymouth,	Pa.	G. J. Durbin.
Dorman, Harry Milton,	Phœnixville,	Pa.	W. A. Dorman.
Doughty, John Thompson,	Millville,	N. J.	A. La Dow.
Duffy, Thomas Anthony,	Carbondale,	Pa.	B. A. Kelly.
Eddy, Eugene Henry,	Loraine,	Ohio.	J. H. Falkins.
Edwards, Manly Bruce,	Bloomsburg,	Pa.	G. P. Ringler.
Eldridge, William Arthur,	Salem,	N. J.	F. Luerssen.
Eshleman, Ellis Good,	Faggs Manor,	Pa.	C. W. Warrington.
Fabian, Asa,	Ottsville,	Pa.	R. H. Fackey.
Faunce, George Castor,	Philadelphia,	Pa.	T. W. Hargreaves.
Fiet, John Jacob,	Philadelphia,	Pa.	H. J. Fiet.
Fisher, John Anthony,	Tremont,	Pa.	J. H. Schultz.
Fox, Harry T.,	Zanesville,	Ohio.	Chappelear & Sons.
Franke, Louis,	Johnstown,	Pa.	C. G. Campbell.
Garritt, Henry James,	Huron,	Ohio.	J. M. Garritt.
Greenberg, Jacob,	Novomirgorod,	Russia,	M. Reissakovitch.
Griest, Joseph Taylor,	Peoria,	Ill.	W. M. Benton.
Gruel, John Edward,	Lancaster,	Pa.	J. C. Long.
Guest, Wilbert Hillman,	Woodstown,	N. J.	W. G. Nebig.
Hampson, William Harvey,	Philadelphia,	Pa.	F. F. Drueding.
Hand, Wilson H.,	Stillwater,	Ok. T'y.	W. R. McGeorge.
Harmony, Edmund Franklin,	Allentown,	Pa.	C. Shoemaker.
Hauber, Christian Henry,	Philadelphia,	Pa.	F. W. Haussmann.
Heinze, George Elmer,	Ashland,	Pa.	A. Schoenenberger.
Heckman, John George,	Meadville,	Pa.	Lindman & Heckman.
Hemberger, Paul Edward,	Dayton,	Ohio.	Jno. N. Prass.
Hilbish, John Henry,	Fredericksburg,	Va.	Jno. C. Greisemer.
Hillebrand, William Gustav,	Philadelphia,	Pa.	W. N. Seary.
Hires, Lewis Moore,	Bridgeton,	N. J.	Reeve & Fithian.
Hughes, Harry Wilbert,	Millville,	N. J.	H. A. Nolte.
Irby, Moreland Russell,	Ashland,	Va.	N. Knight.
Jaeger, William Charles,	Philadelphia,	Pa.	C. H. Bohn,
Jelliff, Glenn Eli,	Mansfield,	Pa.	G. F. Ralston.
Kazanjian, Rupen Hagop,	Armenia,	Adana,	W. L. Matthews.
Kelly, Edward Joaquin,	Philadelphia,	Pa.	L. S. A. Stedem.
Kiefer, William Frederick,	Philadelphia,	Pa.	C. A. Gill.
Kilgus, Harry Edward,	Renovo,	Pa.	M. L. Clay.
King, Lloyd Stanley,	Dayton,	Ohio.	W. P. Graybill.
Kintzer, Harry Augustus,	Womelsdorf,	Pa.	F. T. Landis.
Landauer, Oscar,	Philadelphia,	Pa.	Theodore Sprissler, M.D.
Lehman, Samuel William,	Shippensburg,	Pa.	J. C. Altick & Co.
McCaffrey, Ward Boleyn,	Berkeley Springs,	W. Va.	T. W. Hodgson.
McClure, Charles Nevin,	York,	Pa.	L. K. Slifer.
McDonnell, Wm. Joseph,	Philadelphia,	Pa.	C. P. McDonnell.
McElwain, William Thomas,	Chambersburg,	Pa.	C. W. Keefer.
Mackey, Joseph Quarll,	Avondale,	Pa.	L. C. Funk.
Magee, Michael Vincent,	Conshohocken,	Pa.	T. F. McCoy.
Maier, Frank Joseph,	Woodbury,	N. J.	A. S. Marshall.
Manges, Willis Fastnacht,	Philadelphia,	Pa.	W. H. Gano.
Meredith, Harry Lionel,	Hagerstown,	Md.	Aughinbaugh & Son.
Merz, Alfred William,	Wurtenburg,	Germany.	E. W. Herrmann.

Name.	*Place.*	*State.*	*Preceptor.*
Meuser, Charles John,	Easton,	Pa.	C. L. Bachman.
Michael, George Albert,	Lebanon,	Pa.	C. E. Boger.
Miles, James Bargillar, Jr.,	Helena,	Ark.	
Miller, Bertrand Le Roy,	Liberty,	Pa.	W. A. Musson.
Moeller, Carl Frederick Edw.,		Germany.	W. H. Hickman.
Morgan, Lulu Annette,	Scranton,	Pa.	Mathews Brothers.
Morris, William Torrey,	Penn Yan,	N. Y.	Jas. F. Ross.
Ohliger, Willard,	Wooster,	O.	Zimmerman & Co.
Peiffer, Arthur,	Philadelphia,	Pa.	Steltz & Co.
Piefer, Wm.			
Pursel, Robert Clayton,	Bloomsburg,	Pa.	Moyer Brothers.
Quinn, Francis Denniss,	Johnsonburg,	Pa.	
Rectenwald, Daniel Louis,	Pittsburg,	Pa.	F. W. E. Stedem.
Ricketts, Clarence Emerson,	Kane,	Pa.	E. H. Watkins.
Russell, Walter Harold,	Philadelphia,	Pa.	S. H. Conover.
Saurman, James Spang,	Norristown,	Pa.	Baker & Grady.
Schad, Frank Casper,	Tamaqua,	Pa.	L. J. Steltzer.
Schmidt, Oscar Charles,	Philadelphia,	Pa.	G. A. Barwig.
Scott, John Calvin,	Hamburg,	Pa.	A. J. Rink.
Scott, Levi,	Camden,	Del.	Wilkinson & Wilkinson.
Seabold, Harry Adam Fehnstock,	Annville,	Pa.	W. S. Seabold.
Seip, Charles Louis,	Philadelphia,	Pa.	G. C. Ochse.
Settle, Peter Smith,	Frankford,	Pa.	T. H. Price.
Seward, Frank Gates,	Norwich,	N. Y.	Norwich Pharmacal Co.
Shapiro, Henry,	Vetebsk,	Russia.	F. W. E. Stedem
Siegle, Herman Christian,	Peoria,	Ill.	A. W. H. Reed.
Simcox, Howard Leon,	Philadelphia,	Pa.	Geo. W. Bowen.
Smiley, Frances Jane,	Philadelphia,	Pa.	Wm. Procter, Jr., Co.
Smith, George Carroll,	Pottstown,	Pa.	Eberly Brothers.
Speck, Herbert Arthur,	Bethlehem,	Pa.	Paul Kempsmith.
Stacks, Abraham Homer,	York,	Pa.	C. Perry.
Stolz, Louis,	Syracuse,	N. Y.	
Stout, B. Frank,	Quakertown,	Pa.	N. S. Stiltzer.
Sullivan, James Francis,	Philadelphia,	Pa.	G. H. West.
Sunday, Carlton Pierce,	York,	Pa.	W. Carroll Taylor.
Tucker, Robert Woodlifte,	Hamilton,	Bermuda Is.	Freeman & Pettyjohn.
Weaver, Christian	Naestock,	Denmark.	
Werts, John La Monte,	Renovo,	Pa.	C. P. Landis.
Wilkinson, Harry,	Philadelphia,	Pa.	R. P. Wilkinson.
Williams, Joseph James,	Conshohocken,	Pa.	John W. Pilgrim.
Witman, Charles Daniel,	Middletown,	Pa.	J. W. Renalt.
Witmeyer, Samuel David,	Lebanon,	Pa.	Shinn & Baer.
Wyckoff, Elmer E.,	Rock Island,	Ill.	
Young, Alexander, Jr.,	Jenkintown,	Pa.	S. C. Henry.
Young, Edwin Henry,	S. Bethlehem,	Pa.	Cyrus Jacoby.

SENIORS.

Name.	*Place.*	*State.*	*Preceptor.*
Becht, Frederick,	Philadelphia,	Pa.	Bullock & Crenshaw.
Entwistle, Albert Henry,	Philadelphia,	Pa.	Chas. H. Roberts.
Filer, Burrett Boynton,	Hammonton,	N. J.	J. Frank Mead, M.D.
Jaeger, Chas. Fred'k,	Philadelphia,	Pa.	E. E. Bostick.
Malin, George Lawrence,	Atlantic City,	N. J.	Willard Wright, dec'd.
Peck, Wm. George,	Nottingham,	Eng.	J. Frank Mead, M.D.
Test, Ellwood Allen,	Lancaster,	Pa.	Jno. H. Kerr.

SPECIAL STUDENTS.

Name.	*Place.*	*State.*	*Department.*
Capwell, Harry M.,	Philadelphia,	Pa.	Chemistry.
Carter, F. P.,			Chemistry.
Cavanagh, Frank Arthur,	Ashbourne,	Pa.	Chemistry.
Chapman, Rich'd Henry, Jr.,	Philadelphia,	Pa.	Chemistry.
Crawford, Wm. Henry,	Ashbourne,	Pa.	Chemistry.
Eddy, Eugene Henry,	Lorain,	Ohio.	Chemistry.
Ehman, J. W.,			
French, Rolland Hall,	Salem,	Ohio.	Chemistry.
Gagarn, George,	Wilmington,	Del.	
Jaeger, W. C.,			Chemistry.
Leas, Fred. C.,	Philadelphia,	Pa.	Chemistry.
McMahon, Joseph Alaphonsus,	Lock Haven,	Pa.	Chemistry.
Michels, Victor Clyde,	Albion,	Ill.	Chemistry.
Roberts, John Austin,	Wilmington,	Del.	Chemistry.
Shannon, Sam'l Coward,	Philadelphia,	Pa.	Chemistry.
Stolz, Louis,	Syracuse,	N. Y.	Chemistry.
Suess, Ignatz,	Grand Messeritsch,	Austria.	Chemistry.
Thompson, Samuel,			
Voss, Fred. C.,			
Wyckoff, E. E.,	Rock Island,	Ill.	Chemistry.